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Table of Contents.

Syme Memorial Lecture.[1]

RECENT DEVELOPMENTS IN THE UNDERSTANDING AND TREATMENT OF THYREOTOXICOSIS.

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BEFORE proceeding with the subject matter of my address this evening, I wish to express to the Council of the Victorian Branch of the British Medical Association my sincere thanks for the honour paid to me by the invitation to deliver this the eighth Syme Memorial Lecture. In reviewing the names of those distinguished surgeons who have been my predecessors, I feel very humble in my inability to maintain the high standard they have set, yet proud in my association with them in paying tribute to the memory of Sir George Adlington Syme, a man who not only lived up to the highest traditions of our profession, but set an example of probity, steadfastness of purpose, efficiency and honourable leadership which has been an inspiration to those who were fortunate enough to be associated with him and has provided a standard of professional rectitude and public service that has influenced the whole Australasian medical fraternity.

This was made very evident in the many tributes from New Zealand and all States of the Australian Commonwealth which were presented at the special meeting of the Victorian Branch held on May 12, 1929, so it is only fitting that one from New South Wales should this evening pay homage to his memory and tribute to a man who above all others not only has helped to raise the standard of our profession as a whole, but has played a leading part in establishing Australian surgery on the high plane it holds today.

His is a memory which the passage of time can never efface.

When Syme retired from active professional life in 1924 the Council of the Victorian Branch of the British Medical Association decided to establish a Foundation in his name to be applied to the advancement of surgical science, and as a result we have this triennial lecture.

The surgical treatment of toxic goitre as it stands today was initiated in Melbourne by Sir Thomas Dunhill and developed by Sir Alan Newton. For many years Victorians were far ahead of the other States in the surgery of thyreotoxicosis, and it was not until about 1920 that opportunities came my way to overcome the prejudices of the physicians as regards surgery in this condition.

Strangely enough, with the advent of the "thio" compounds, introduced by Astwood in 1943, and the realization that for the first time we had a drug which could directly control a hormone, the role of my activities was changed, and it became my mission to demonstrate that the majority of patients could be cured of Graves's disease by medical treatment. Surgery will never be displaced from a major place in the cure of thyreotoxicosis, as some 15% of patients with primary Graves's disease require operation to remove persistently enlarged thyreoid glands, and with all secondary types of toxic goitre the patients require surgery to effect a cure of their hyperthyreoidism.

It is essential to realize that thyreotoxicosis is a malady which affects every tissue in the human body and that it is not a disease affecting only the thyreoid gland.

[1] Delivered at a meeting of the Victorian Branch of the British Medical Association on September 6, 1950.

J. H. Means, in a recent article, describes Graves's disease as "a widespread and complex constitutional disorder involving, besides the thyroid, other endocrine glands, the tissues of the orbit, the spleen, the thymus and the lymphatic, reticulo-endothelial, hæmopoietic, muscular, nervous and very likely other bodily systems". In his recent book on "The Thyroid and its Diseases", Means stresses this aspect of the complaint and presents a masterly summary of experimental and clinical work on this disease which will afford a basis for my address this evening.

General Considerations.

McCarrison believes that in the human the thyreoid attains its maximum size just prior to the age of puberty, which is thus the time of maximum load upon the organ, a consideration to be kept in mind in relation to the colloid enlargement seen so frequently at puberty. In the normal person the thyreoid is neither visible nor palpable, but in very thin subjects with long necks it may become so, especially in women prior to menstruation and in pregnancy, also after periods of emotional stress. Frequently such persons are told by their doctor that they have a goitre, whereas their fears in this respect should be allayed by the explanation that the condition is purely physiological.

The gland has a very abundant blood supply, and although its normal weight is only 20 to 25 grammes, the total blood volume of the individual passes through the gland about once an hour; in hyperthyreoid states the flow is greatly increased. The thyreoid has a very rich nerve supply from both the sympathetic and parasympathetic, especially about the arteries, and although many fibres wander abundantly among the follicles, there is no evidence of any direct contact with parenchymal cells. As to what is the exact function of this nerve supply, no agreement has yet been reached, although a great deal of experimental work has been done. It is possible that there is no true secretory function, but the vasomotor innervation may govern the delivery of hormone to the blood-stream and may regulate its production by governing the oxygen supply to the gland cells, especially so since each follicle has its individual artery. The follicle is the secretory unit in the thyreoid gland, the cells forming the hormone which is stored in the lumen of the follicle. Normally the follicles vary in size, apparently depending on whether they are in the colloid storage phase or in that of colloid release, but in disease the extremes are found—for example, great distension in colloid goitre and a practically empty state in acute hyperthyreoidism. The epithelium of the follicle is normally only one cell deep, the cells being cuboidal in shape, but it varies according to the activity of the gland. A technique has been developed for ascertaining the epithelial cell height, and this is now used as an index of functional activity.

The Colloid.

Within the lumen of the normal follicle is the colloid, which is to be regarded as the actual secretory product of the gland. It has been pointed out that "thyreoid colloid is the only instance in the whole animal kingdom where a supposed physiological secretion is first eliminated from cells in one direction then absorbed by the same cells and eliminated in the reverse direction".

It is of interest to note that the viscosity of the colloid diminishes after the injection of thyreotropic extracts from the pituitary and for a short period after the exhibition of iodide. When the latter is given for a long period the viscosity of the colloid is increased. We may note the clinical application of these facts in the soft hyperplastic thyreoid of acute Graves's disease with its empty follicles, as contrasted with the definite firming of the gland due to colloid storage after two or three weeks' administration of iodine and its stony hardness after prolonged or excessive iodine medication.

The question of when the fœtal thyreoid assumes secretory activity is of importance with the increasing use of "thio" compounds in the treatment of thyreotoxicosis during pregnancy. Colloid production was taken as evidence of thyroid activity, and as this does not become apparent until about the sixth month of intrauterine life, this was regarded as the time when the fœtal thyreoid began to function. However, with the experimental use of radioactive iodine, it has been shown that the fœtal thyreoid begins to collect iodine about the fourteenth week, and it may be assumed that this ability to collect radioactive iodine is synonymous with functional activity, even though colloid storage is not evident until a later stage. Both radioactive iodine and thiouracil or its derivatives have been used in the treatment of thyreotoxicosis up to the seventh month of pregnancy, without any ill effect on the child, but if "thio" compounds are used in the last two months, hyperplasia of the child's thyreoid may occur, and a few cases of actual cretinism have been recorded. It does not seem to be generally known that during pregnancy the activity of the maternal thyreoid gradually increases as the child develops, and in the last six to eight weeks a basal metabolic rate of +15% to +20% is a normal level. If hormone production in the maternal thyreoid is inhibited in these later stages, a similar effect occurs in the fœtal thyreoid, and a frustration hyperplasia in both mother and child is to be expected—a condition of affairs exactly analogous to the old observation that a myxœdematous mother is apt to produce a cretinous child.

It is known that thyreoid colloid is protein, but whether it is a single protein in the form of thyreoglobulin, as is generally thought, or a mixture of proteins has not yet been fully determined. Thyreoglobulin is the only protein which contains iodine, and it is carried exclusively by two of its component amino-acids, thyroxine and di-iodotyrosine. Unlike other organs such as the liver, the adrenals *et cetera*, the thyreoid cells do not store their product within the cells, but it is stored in the follicle.

The increasing study of nuclear and other intracellular phenomena is opening up a vista which may well lead to the proper understanding of the hormone production of the thyreoid. With increased cellular activity there is an increase of the mitochondria, upon which lipoids accumulate, and with involution they diminish so that lipoids return to the cytoplasm, a process which would account for alteration in cell permeability and the behaviour of the cell in relation to its environment. Investigation of the Golgi apparatus, secretory globules and intracellular enzymes, such as the peroxidase activity already demonstrated, is going ahead and promises very interesting results for the near future.

One further fact of practical importance regarding colloid is that its formation can proceed in the absence of a supply of iodine; this occurs in iodine-want goitres, but the colloid formed has no hormone-like action on body tissues. When iodine is given in such cases there is a rapid iodination of the colloid, which then acquires physiologic activity, and thus we have the explanation of clinical improvement in certain types of simple goitre.

The Thyreoid Hormone.

Since Harington in 1927 showed that thyroxine could be synthesized, our knowledge of this substance has increased enormously, and his statement in 1944—that it "is the only physiologically active substance which can be isolated in the pure state from the thyreoid gland and to all intents and purposes therefore can be regarded either as the complete hormone or at least the business portion of it"—has now been generally accepted. The synthesis of the thyreoid hormone within the gland appears to depend on two independent processes, namely, the iodination of tyrosine and the synthesis of protein or colloid. As already noted the latter process can proceed in the absence of a supply of iodine, but colloid so formed contains tyrosine radicles capable of iodination. Iodine reaches the gland as iodide, which is oxidized to elemental iodine by enzyme action and combines with tyrosine to form di-iodotyrosine within the thyreoglobulin molecule; then two di-iodotyrosines are coupled to form thyroxine, a process which only the thyreoid cells can effect.

The iodinated thyreoglobulin is stored in the colloid, but before entering the blood-stream it undergoes further enzymatic splitting into more soluble polypeptides containing thyroxine. In this form the hormone can diffuse either direct from the cell or across it from the follicle into the blood, where it is incorporated in the molecule of a plasma protein and transported throughout the body.

The avidity of the thyreoid for iodine makes one realize that there must be some method of storage, possibly by adsorption on protein, as it is not all utilized immediately in thyroxine production, although this process is a continuous one under normal conditions with an ebb and flow of the stored colloid according to the tissue requirements.

Means classes the activities of the thyreoid hormone under ten headings, which we may review briefly.

1. Calorigenic action. This refers to the maintenance of a normal metabolic level allowing of fluctuations to meet changing physiological needs and is an activity now well known to clinicians.

2. Action upon growth, maturation and differentiation of tissue. This is also well known in its major manifestations, especially in dwarfism of the cretin, but its minor effects are apt to be overlooked, especially the effect on skin, hair, nails and eruption of the teeth. Also there is a pronounced effect on bony development, as in hypothyreoidism there is a delay in the appearance of centres of ossification and consequently in epiphyseal union. Conversely, in adolescents with hyperthyreoidism there is increased growth.

3. Action on body water, salts and proteins. Lack of thyreoid hormone with consequent decline in the rate of oxidation leads to a storage of water, salts and protein in the body with a reduction in plasma volume and an increase in the protein concentration of the cerebro-spinal fluid. Conversely, any excess production of thyreoid hormone acts in the opposite direction, as does its exhibition in the subthyreoid patient. One of its most striking results in such cases is the diuretic effect, which helps materially in reducing the weight of the individual. F. B. Byrom showed that in normal subjects the water lost in this diuretic action of thyroxine came from intracellular sources, as it contained more potassium than sodium, and potassium is the chief base of intracellular fluid; but in myxœdematous subjects there was an excess of sodium, which comes from extracellular sources. Coincident with diuresis there is a loss of protein as indicated by the nitrogen balance.

4. Action on carbohydrate metabolism. Excessive production of thyreoid hormone depletes the liver of its glycogen and if continued does some injury to the liver cells, which may become unable to store glycogen. There is an accelerated absorption of sugars and starches in the alimentary tract and increased oxidation of dextrose in the tissues, which leads to depletion of glycogen storage. These findings are of clinical significance, especially in long-continued hyperthyreoidism, which is often associated with liver damage affecting the detoxicating function, and this is of importance to the surgeon.

5. Action on lipoids. This is indicated by the elevation of the serum cholesterol level in myxœdema and its reduction in hyperthyreoidism. Reference has already been made to the intracellular activity of the mitochondria and their balancing action on lipoids.

6. Action on the nervous system. The subthyreoid individual lives on a low emotional level, cerebrates slowly and has a slow reaction time to stimuli, whereas the hyperthyreoid person has heightened emotions even to a state of instability and increased irritability, and may proceed to a gross derangement of cerebration. There is also increased vasomotor, peristaltic and sweat-gland activity, as a result of imbalance of the sympathetic nervous system such as is found in cases of neuro-circulatory asthenia.

7. Action on the muscular system. Changes occurring in the metabolism of creatin run practically parallel to the metabolic rate and may be taken as indicative of changes occurring in the muscles. The myasthenia which is such a notable clinical expression of hyperthyreoidism is dependent on the metabolic and biochemical changes occurring in the musculature and is particularly enervating when imbalance of the eye muscles occurs. Increased muscle tone and exaggerated reflexes also occur, and in some cases muscle wasting may simulate that met with in an advanced case of progressive muscular atrophy.

8. Action upon the circulatory system. Increased metabolism is associated with an increased mass movement of blood as a consequence of the rapid heart action, the dilatation of peripheral vessels and the increased stroke volume of the heart. This is not wholly the result of increased metabolism, and there is good evidence to believe that excess thyroxine has a direct effect on heart muscle. It has been pointed out that with hyperthyreoidism the circulation is working less efficiently than is the case when metabolism is increased as a result of muscular effort. It is probable that part of this effect on the circulation may result from the excitory action of thyroxine upon the adrenal medulla. Long-continued hyperthyreoidism undoubtedly leads to degenerative changes in the heart musculature.

9. Action of the thyreoid hormone on the thyreoid gland. This is not as strange as it sounds, for a rise in the level of circulating thyroxine diminishes the secretory activity of the thyreoid cells, despite the fact that the general metabolism of these cells may be increased, as is the case with all the body tissues. In hypothyreoid states a frustration hypertrophy of the gland may occur with increased storage of colloid deficient in hormone.

10. Action on other endocrines. This is a fascinating study and an enormous volume of experimental work has been done on the interrelationship and activities of the various endocrines. As evolution has proceeded the pituitary has gained a major control of the other endocrines, but in turn its activities through its tropic hormones is dependent to some extent on the other endocrines. This is particularly so with the thyreoid, and normally the balancing of the thyreotropic (or thyreoid-stimulating hormone) of the anterior pituitary lobe is determined by the amount of thyroxine in the blood-stream. An excellent example of this action is seen when hormone production in the thyreoid is prevented by thiouracil compounds; a gross hyperplasia of the gland occurs as a result of the excessive and unbalanced production of thyreotropic hormone from the pituitary, the so-called goitrogenic action.

Concerning the posterior pituitary lobe, there is no positive relationship so far determined, but the diuretic action of the thyreoid hormone may be linked up with some interrelation between thyreoid and posterior pituitary lobe.

With regard to the adrenal, we realize that certain manifestations are common to disorder of the thyreoid and adrenal, and with hypofunction of the adrenal, myasthenia and pigmentation may occur similar to that in hyperthyreoidism. There appears to be some sort of antagonistic action between these glands, whereby the hormone of one gland protects against ill effects of over-production of the other, and Marine has suggested that hypofunction of the adrenal cortex may play some part in the genesis of Graves's disease. Also we have the old observation of Goetsch that thyreotoxic patients are sensitive to adrenaline, and we know that patients with hypofunction of the adrenal cortex are more sensitive to thyreoid hormone than are normal persons.

The eosinophile cell has come to be regarded as a good index of function of the adrenal cortex, and it is interesting to note that in thyreotoxicosis the eosinophile cells fall in number, but during treatment with the "thio" compounds they increase very quickly, even as high as 15% to 20%. It has been observed in a large series of patients with Addison's disease that a great number have a past history of thyreotoxicosis, which lends support to the view that there is some antagonistic action between the thyreoid and the adrenal cortex.

The relationship between thyreoid and thymus is possibly antagonistic also, and the persistent thymus in

cases of Graves's disease has long been known. What the exact relationship is between them has not yet been determined.

Clinically it would seem that there is some association between the thyreoid and the gonads, as in women with hyperthyreoidism there is frequently some disturbance with the menses or even amenorrhœa, and there may also be a tendency to abortion or a decrease in fertility. The latter may occur in hypothyreoidism, and there is also a tendency to menorrhagia. Some experimental work suggests that the ovarian hormone may inhibit the thyreotropic hormone of the pituitary, and in certain cases there is no doubt that the exhibition of ovarian hormone helps materially, especially when exophthalmos or so-called "localized pretibial myxœdema" is present. Testosterone stimulates thyreoid activity, probably as a direct effect, but it may act through the pituitary.

In the case of the pancreatic islets there is no doubt that hyperthyreoidism aggravates *diabetes mellitus* and can inhibit the action of insulin in these cases. There is evidence that total thyreoidectomy is helpful in controlling some types of diabetes, which then respond to smaller doses of insulin.

The Thyreoid Hormone and Vitamins.

An enormous amount of work has been carried out on the subject of the thyreoid hormone and vitamins, but most of it has been animal experimentation, and it is important to realize that results so obtained are not always applicable to the human subject. However, there is sufficient clinical evidence to determine that there is a clear relationship which is of importance in the treatment of thyreoid disorders.

Vitamin A.—In animals a deficiency of vitamin *A* appears to cause hypertrophy of the thyreoid, the suggestion being that it induces some alteration in the thyreoid cells preventing the proper utilization of iodine, so that the gland behaves as if there were a "relative" iodine deficiency. The thyreoid cells are epithelial, and as vitamin *A* deficiency is a factor in degenerative changes in epithelial structures, it is likely that the animal experimental findings are applicable to the human being; but the proportion of change in epithelial structures due to lack of vitamin *A* and that due to dysfunction of the thyreoid in its hormone production cannot be determined. Vitamin *A* may counteract to some extent the action of the thyreotropic hormone of the pituitary, and there is evidence that it has a beneficial effect on the loss of liver glycogen associated with hyperthyreoidism.

Vitamin B.—The administration of yeast in thyreotoxicosis has long been known to exercise a beneficial effect, and animal experiments show that it delays the onset of liver damage in long-continued hyperthyreoidism and will prevent the depletion of liver glycogen. On the whole there does not seem to be any question that increased *B* group vitamins are required in these cases, especially when the nervous system exhibits major manifestations in the symptomatology.

Vitamin C.—There is no doubt that thyreotoxicosis increases the demand for vitamin *C* as the urinary excretion level is below normal, whereas after thyreoidectomy it rises to a normal level. Deficiency of this vitamin causes an increase in the size of the thyreoid gland, increase in the height of the follicular cells, increase in the interfollicular cells and decrease in colloid, all of these changes being greater in the chronic than in the acute deficiencies.

Vitamin D.—It is well known that in thyreotoxicosis there is excessive loss of both calcium and phosphorus, and it is probable, although not proven, that vitamin *D* added to the dietary in such cases will be of some benefit, especially if there has been any alimentary upset which may hinder the absorption of these substances.

On the whole, it seems that the addition of a standardized mixed-vitamin preparation to the dietary of the thyreotoxic patient is beneficial.

Exophthalmos.

Exophthalmos is one of the mysteries of Graves's disease. If it is a direct result of thyreotoxicosis it should be present whenever this condition is manifest, whether it be the acute hyperplastic goitre of Graves's disease, the toxic adenoma, or those pathological conditions in the thyreoid associated with a secondary type of thyreotoxicosis. It has been thought that ophthalmopathy is due to or associated with an excessive production of thyreotropic hormone, chiefly because of its occurrence in animal experiments after injection of extracts from the anterior pituitary lobe, but this does not explain why it is limited to Graves's disease alone out of the several varieties of thyreotoxicosis, nor does it offer any explanation of this condition's arising independently of any toxic thyreoid state or of why on occasions only one eye should be affected.

In theory a total thyreoidectomy should always be followed by exophthalmos, owing to an excessive production of thyreotropic hormone from lack of balancing by thyroxine, but in the many hundreds of total thyreoidectomies I have performed I have not seen it happen, even though *Thyroideum Siccum* has been withheld until definite myxœdema develops. It will be seen from this that I do not subscribe to the view that operation should not be performed if any degree of exophthalmos is present. Normally the thyreotropic hormone stimulates the thyreoid gland to increased production of thyroxine and in so doing becomes inactivated, but it has been found that the gland of Graves's disease can inactivate more thyreotropic hormone than the normal gland, and also that the thymus and lymphoid tissue can inactivate it. The fact that the ocular muscles are invaded by lymphocytes links up with this thymo-lymphatic dyscrasia and must be of some import, but at present no adequate explanation of the relationship has come forward. There is no doubt that there is an increase of orbital fat and of water content in the orbital tissues, in addition to the changes in the muscles leading to myasthenia and thus to lessening of the muscular pull to hold the eyeball back against the increased content of the orbital cavity. In cases of progressive ophthalmopathy thyreoid extract has been used with some degree of success in checking the condition, and I have given with it minimal doses of methyl thiouracil and in some cases after the menopause small doses of stilbœstrol and found greater benefit than with thyreoid extract alone.

The Toxic Adenoma.

When Plummer postulated the toxic adenoma, Means stated that he felt some diffidence in accepting his views. Since the carrying out of the experimental work with the uptake of radioactive iodine in thyreoid abnormalities, along with consideration of the mean cell heights of the acini, and estimations of the basal metabolic rate, he now considers that a toxic adenoma is a definite entity and that hyperthyreoidism in such cases is entirely different from that in Graves's disease; the latter is a direct result of excessive production of thyreotropic hormone from the pituitary, whereas the toxic adenoma is not under hormonal control. It may be presumed that as the thyroxine production of the adenoma increases the thyreotropic hormone diminishes, thus cutting down the hormone production by the thyreoid parenchyma and maintaining the euthyreoid state. However, as the activity of the adenoma increases the time comes when its thyroxine production rises above the normal requirements of the body, and thyreotoxicosis supervenes with a rise in the basal metabolism. In such cases the amount of radioactive iodine taken up in the adenoma may be ten to twenty times that of the surrounding gland tissue. Means refers to these toxic adenomata as "hot" nodules, in contradistinction to the "cold" or non-secreting nodules which may be found in the hyperplastic glands of Graves's disease. I have frequently noticed in the latter cases that when resolution of the hyperplasia has been induced by a "thio" compound, an adenoma shows up which had not been palpable in the enlarged gland. It is quite likely that "hot" nodules may be associated with a general hyper-

plasia of the gland and provide an augmentation of the thyreotoxicosis.

Some Aspects in Diagnosis.

From what has been said it is not difficult to understand the symptomatology of hyperthyreoidism, and in an established case the diagnosis is evident. However, certain types of neuro-circulatory asthenia (anxiety neurosis, sympathetic imbalance *et cetera*) present difficulty in diagnosis, especially if there is any enlargement of the thyreoid gland. Estimation of the basal metabolic rate in such cases is apt to be misleading unless carried out by an experienced and skilled biochemist. Various metabolimeters are now marketed, but unless they are used by a well-trained person who not only understands the machine but realizes what a true basal condition is, they can give most fallacious results. In taking a basal metabolic estimation all the factors which may go wrong lead to a high reading and not to a low one, so that a single low result is much more likely to be correct than a single high one. If there is any doubt about the report a positive diagnosis can be made by observing the patient's reaction to adequate doses of one of the thiouracil derivatives, which in the thyreotoxic patient will lead to a definite amelioration of symptoms within three weeks. If this beneficial reaction does not occur the patient's symptoms are due to some cause other than hyperthyreoidism. I have found this test much more reliable than that of the diagnostic use of iodine.

However, there are cases in which some form of neurasthenia is associated with hyperthyreoidism, but control of the latter will relieve the former.

Patients with hypertension and thyreotoxicosis also present difficulty at times in diagnosis, but again with "thio" compounds relief of general symptoms occurs, and the pulse pressure falls as does the systolic blood pressure, even though a high pulse rate is maintained. If symptoms are due to hypertension only then no clinical improvement occurs.

Fever, of course, elevates the metabolic rate, but it should be routine practice to determine the patient's temperature before a metabolic test is performed.

A rare cause of increased metabolic rate one may meet with is a non-toxic thyreoid in a patient with leuchæmia, but other presenting symptoms and signs should lead one to have a blood examination carried out.

Control of Hyperthyreoidism.

The value of iodine is well known in the preparation of the toxic goitre patient for operation, but the mechanism involved in its beneficial action was not understood until recent years. It is now clear that the fall in basal metabolism induced by iodine corresponds to that of thyroxine decay. Iodine has no action on thyroxine already formed, but acts in the thyreoid gland by instituting storage of the depleted colloid and reducing the activity of the thyreoid cells, thus inhibiting the formation of the hormone, and recent work indicates that it also inhibits the action of the thyreotropic hormone of the anterior pituitary lobe upon the thyreoid cells. It is probable that the restoration of free iodide in the blood-stream has a beneficial effect on the general body tissues. However, it must be remembered that this effect continues up to a certain point only; after this the symptoms of hyperthyreoidism recur, but not to the same degree as they do when the administration of iodine is stopped. The explanation given is that long-continued iodine medication holds the hyperthyreoidism at a lower level than would be the case otherwise, and the malady smoulders on as a chronic condition until such time as it is completely burned out or until a nervous or cardio-vascular breakdown compels medical attention.

Although only about 0·2 milligramme of iodine is needed daily to maintain the output of thyroxine in a normal individual, the effective dosage required in thyreotoxicosis is 6·0 milligrammes daily which is contained in one minim of Lugol's solution; any dosage in excess of this is redundant and may be harmful, although custom has ordained up to thirty times this amount daily. Lugol's solution is the iodine preparation most used, but potassium iodide in small doses, or any other iodine compound, is equally effective. It was thought that as di-iodotyrosine was a normal constituent of the thyreoid it might be more effective than iodine in other forms, but this is not the case.

With the introduction of thiourea and thiouracil or its derivatives, tremendous interest in their control of hyperthyreoidism was evoked, and a voluminous literature, both experimental and clinical, has been produced over the last seven years in particular. It is clear that the response obtained is different from that of iodine, which is specific for hyperthyreoidism; with the "thio" compounds it is non-specific, and with their continued use any organism possessing a functioning thyreoid gland can be deprived of the thyreoid hormone. The fall of the metabolic rate is again that of thyroxine decay, as the formation of thyreoid hormone is blocked, and any stored or circulating thyroxine has to be utilized before the effect of the drug becomes manifest. In normal individuals with hormone stored in the follicles of the gland, it takes many weeks and even months before a myxœdematous level is induced; but in Graves's disease, where there is no colloid storage, clinical results become obvious within five to ten days and a *minus* metabolism frequently becomes evident in six to eight weeks. Although the "thio" compounds act as anti-thyreoid agents in thyreotoxicosis, one must remember that they are also goitrogenic and that the hyperplasia of the gland is apt to increase; in a gland not previously hyperplastic this condition will develop, as the thyreoid-stimulating pituitary hormone still continues in excess for some time and a frustration hyperplasia results.

Studies on the uptake of radioactive iodine show that as much as 95% of a tracer dose of iodine will be taken up by the thyreoid in a case of untreated thyreotoxicosis, but after thiouracil is given the uptake is not more than 7%.

It is a well-established fact that the prior administration of iodine delays the response to the "thio" compounds owing to the involuting action of iodine on the gland and the storage of hormone in the follicles.

Experimentally it is evident that with the coincident administration of iodine and "thio" compounds an involuting action can occur in the hyperplastic gland of Graves's disease; but clinically the results have not been as promising as was expected except perhaps in the later stages of treatment. Then only minimal doses of the "thio" derivative are being administered and some degree of iodine uptake is developing for the production of a controlled amount of thyroxine, so that both the involuting and the iodinating actions of iodine can come into play.

This consideration led to the introduction of iodinated thiouracil compounds, which have recently been tried in a series of cases of hyperthyreoidism. With iodinated thiouracil "the responses simulated qualitatively those following iodide therapy more than those which thiouracil produces". The methyl combination was much less effective than its non-methylated analogue. The propyl compound afforded no significant benefit. On the whole the results have been relatively disappointing with these iodinated compounds.

In many clinics the use of thiouracil and its compounds is restricted to the control of hyperthyreoidism as preparation for operation—that is to say, as "short-term" therapy of two or three months' duration; by then the basal metabolism has fallen to normal and the patient's general physical condition has improved. The technical difficulties at operation were increased as the glands were soft and very vascular, so it was decided to use iodine for two to three weeks before operation for its involuting action on the gland, which became firmer, less vascular and easier to handle. This observation was made independently in my own practice some three or four months before report of a similar procedure was published from the Lahey Clinic. There is ample evidence now to prove that such pre-operative preparation with "thio" compounds has reduced the mortality of operation to about one in a thousand, or even less in skilled hands, and has rendered two-stage operations unnecessary.

The question was raised in the early days of "thio" therapy whether a cure of thyreotoxicosis could be obtained without surgery. After some experience with these anti-thyreoid compounds it became clear that in certain cases and with "long-term" therapy an apparent restoration of the patient to normal did occur.

Upon close analysis it was found that this result was achieved in persons with acute primary thyreotoxicosis, provided treatment was instituted within three or four months of the onset of symptoms and before a large hyperplastic gland developed. With the use of methyl thiouracil and adjuvant therapy over a period of eight to eighteen months, a 64% rate of cure in such cases is obtained—that is to say, the patients reverted to a normal condition in all respects and have remained so for at least two and up to five years after ceasing treatment. In 2% of cases treatment had to be abandoned because of toxic reactions or lack of cooperation, and operation was carried out. In the other 34% the patients showed some evidence of their old thyreotoxicosis, mainly some degree of prominence of the eyes, myasthenia, nervous instability or a persistently enlarged gland, the latter accounting for 15% of the total. As recurrence of symptoms was observed in 5% of the patients originally treated, they were investigated, and it was found to have happened only in those who had persistently enlarged glands; the recurrence developed within nine months after treatment was stopped. Although such patients responded well to further therapy it was considered advisable to submit them to operation, and finally the balance of 15% with an enlarged gland were also subjected to surgery although they had no recurrence of symptoms. Since then, however, I consider it unnecessary to operate in these cases unless recurrence of symptoms does take place. Examination of these glands after removal showed that in those from patients who had recurrence of toxicity there were many areas of hyperplasia, although the greater part of the gland showed ample colloid formation. In the majority of those from patients who had had no recurrence the gland follicles were full of colloid, presenting the picture of a resting phase, and no areas of hyperplasia could be demonstrated.

As Lahey contends that "thio" compounds do not cure hyperthyreoidism and recommends operation after a short term of treatment, it is evident that he has not allowed sufficient time with a low-dose maintenance therapy to permit Nature to restore a normal pituitary-thyreoid balance and thus bring about a cure. It has been found that when "long-term" therapy has been decided upon, it is advisable to reduce the dosage of the drug as soon as it is evident that control of hormone production has been achieved. This on the average occurs in about five weeks. The maintenance of a zero or mild *minus* metabolism for a minimal period of four months is advisable, but during this period if there has been any exophthalmos or gland hyperplasia the anterior pituitary lobe must be balanced by giving thyreoid extract in small doses. It seems to take several months before the excessive output of thyreotropic hormone from the pituitary subsides, and this is helped, too, by regular mild sedation and freeing of the patient as far as possible from any mental stress, with consequent reduction of stimuli from the hypothalamus to the pituitary and diminution of its output of thyreotropic hormone. G. W. Harris, in discussing "The Hypothalamus and Endocrine Glands" in the *British Medical Bulletin* (Volume VI, Number 4, 1950) just to hand, states that "one of the striking facts emerging from recent work is the emphasis on emotional and psychological factors in the control of endocrine secretion", a state which is frequently overlooked in the treatment of toxic thyreoid conditions.

Following the suggestion made by David Lehr, of New York, in September, 1948, I used a combination of methyl and propyl thiouracil in the treatment of thyreotoxicosis. The choice of these compounds was made as a result of experimental work by McGinty and co-workers, who showed that in dogs methyl thiouracil reached a peak level of 3·6 milligrammes *per centum* in the blood in one and a half hours after ingestion, whereas propyl thiouracil reached a peak of 3·0 milligrammes *per centum* in three hours. It was thought that a summation effect would occur increasing the peak level over at least three hours. The clinical results bear this out, as a much quicker control of the hyperthyreoidism is obtained and the results are an improvement on those with methyl thiouracil alone.

As has been pointed out, thyreotoxicosis affects the body tissues as a whole, and it is essential to remedy not only the imbalance of thyreoid secretion but also any or all other functions or tissues that have been deranged. Ancillary treatment by regular sedation, mental as well as physical rest, correction of dietary deficiencies, building up of glycogen storage *et cetera*, is almost as essential in the securing of a satisfactory result as is the control of the excessive hormone production of the thyreoid.

Conclusion.

It is hoped that this review of factors influencing the behaviour of the thyreoid gland may help to a better understanding of the rationale of treatment of its disorders, particularly in the thyreotoxic conditions. Now that work has actually been commenced in Australia on the building of a cyclotron, it will not be many years before we have liberal supplies of radioactive iodine. Already there is a good understanding of its use and value in toxic goitre, and results in many cases are very promising. However, R. H. Williams in an article published last year on the "Selection of Therapy for Individual Patients with Thyrotoxicosis", after a critical consideration of all the factors involved and results obtained over a period of five years, places "thio" therapy as first choice, with radioactive iodine a close second and surgery some distance away as last. He considers that operation is best for a large nodular gland or when rapid recovery is the main objective despite the risks.

With regard to the question of rapid recovery, one should take into consideration the economic aspect; in the suitable case "thio" therapy is worthy of trial, for practically every patient can carry on treatment without interruption to his work other than a visit to the doctor some eight to ten times in the year.

Rapid control of symptoms is obtained, after which treatment is taken only twice daily during the maintenance period.

If operation is ultimately deemed advisable, it can be carried out at the patient's convenience when the physical condition is first class and with comparatively little risk, no post-operative reaction, a stay in hospital of at most ten or twelve days and a rapid convalescence.

A SIMPLE METHOD FOR ESTIMATION OF 17-KETOSTEROIDS IN URINE.[1]

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DURING the last decade interest in the excretion of 17-ketosteroids in various clinical conditions has led to an increasing demand for such investigation to be performed in hospital laboratories. Because the early methods were very lengthy and it was difficult to obtain pure crystalline androsterone for the standard for colour comparison, assays of 17-ketosteroids have been carried out in only a few of the larger laboratories. The number of requests for these tests has risen to such an extent that these laboratories have been forced either to curtail their own work, or, reluctantly, to refuse to comply with them. The present paper describes a simpler method, which can be employed in the smaller laboratories, and which has the additional advantage of substituting an artificial colour standard for the androsterone.

[1] This work was made possible by a grant from the National Health and Medical Research Council of Australia.

Originally we used a modification of the method of Dingemanse, Borchardt and Laqueur (1939). In this method there are three main stages: (i) hydrolysis and extraction, (ii) fractionation and (iii) colorimetric estimation. Friedgood and Whidden's modification of the Zimmermann colour reaction was used for the colour development.

In stage (i) the total twenty-four-hour specimen of urine is hydrolysed by boiling with concentrated hydrochloric acid for ten minutes, followed, after rapid cooling, by extraction with carbon tetrachloride in a boiling water bath for forty minutes. This extraction process is repeated twice.

In stage (ii) the residue, after distilling off of the carbon tetrachloride, is dissolved in benzene. The benzene extract is washed twice with saturated sodium bicarbonate solution to remove traces of hydrochloric acid. The phenols are then removed from the extract by washing five times with twice normal sodium hydroxide solution, and finally it is washed with water to remove traces of sodium hydroxide.

After the benzene solvent has been distilled off, the residue is extracted with four or five small volumes of ether, and the ethereal extracts are run through a sintered glass filter and the ether is then distilled off. The residue is taken up in absolute alcohol, the final volume being 25 millilitres. If the solution is deeply coloured, treatment with a small amount of animal charcoal has been found to remove pigments, but not the 17-ketosteroids. Suitable aliquots are used for the colorimetric estimation.

In stage (iii) several aliquots (0·25, 0·5, 0·75 and 1·0 millilitre) of the alcoholic extract are evaporated to dryness in a boiling water bath. After cooling, colour is developed by the addition of m-dinitro-benzene and alcoholic potassium hydroxide. The colour develops gradually and reaches a maximum after seventy-five minutes at 25° C. A series of volumes of 0·01% androsterone solution in absolute alcohol are prepared in the same way at the same time. The pink colour developed in both the extract and the standard solution is admixed with a yellow or brown colour and cannot be read in a visual colorimeter without the use of a green glass screen.

From this summary of the method, the amount of labour and the time involved can be gauged.

Artificial Colour Standard.

The difficulty in obtaining pure crystalline androsterone has been overcome by the use of a solution of cobalt chloride. Mr. H. Holden (Walter and Eliza Hall Institute of Medical Research) found that the colour of a solution of cobalt chloride prepared by dissolving two grammes of pure cobalt chloride in one millilitre of normal hydrochloride acid and diluting to 100 millilitres with distilled water, compared satisfactorily with that developed by treating 0·5 millilitre of 0·01% androsterone solution as already described. The comparison must be made in a dark room and the colours viewed through a green glass screen.

Modifications of the Original Method.

In 1943 Robbie and Gibson eliminated some steps in the Dingemanse procedure, but the method was still tedious.

More recently Drekter *et alii* (1947) described a rapid method for the determination of total 17-ketosteroids in urine involving use of very small volumes for each assay. Ten millilitres of urine are hydrolysed with concentrated hydrochloric acid and then extracted in a separating funnel with ether only. The ether extract is washed once with sodium hydroxide solution and once with water. Five millilitres of this extract are then assayed by the Zimmermann m-dinitro-benzene reaction.

At the time our attention was drawn to this method we were using a Klett visual colorimeter, and the intensity of colour and volume of solution were unsatisfactory for use in this type of colorimeter. We therefore modified the method in the following way to satisfy these conditions.

Modified Drekter Method.

Stage (i). The total volume of urine collected for a period of forty-eight hours is thoroughly mixed and then halved. One-tenth of the average twenty-four-hour volume is hydrolysed by the addition of concentrated hydrochloric acid in the proportion of 15 millilitres to 100 millilitres of urine. The mixture is gently boiled for fifteen minutes in a large Erlenmeyer flask containing a few pebbles and with a small funnel resting in the neck to prevent too great concentration. The specimen is cooled immediately in running tap water.

Stage (ii). The hydrolysate is extracted in a separating funnel with a total volume of ether equal to two to four times its volume. The ether is divided into three portions, half of the total volume being used for the first extraction and one-quarter for each of the two subsequent extractions. Shaking of the separating funnel about 100 times, with opening of the tap frequently to release pressure, has been found to give a quantitative extraction of the 17-ketosteroids. Inversion and gentle shaking produce less emulsification than vigorous shaking. The combined ether extracts are washed twice with five-normal sodium hydroxide solution, the volume for each washing being half that of the urine which was used; this is followed by at least two washings with large volumes of distilled water until the ether extract is free from sodium hydroxide. The washed ether extract is transferred to a 500-millilitre distillation flask and the volume reduced to about five millilitres by distilling off the ether in a hot water bath. The extract is then transferred quantitatively to a 50-millilitre bolt-head flask by Pasteur pipette and teat, small volumes of ether being used to wash out the flask. The ether is finally completely removed by immersing the flask in a hot water bath and blowing a current of air through the flask to dry the residue completely. The residue is dissolved in absolute alcohol and made up to a volume of five millilitres.

Stage (iii). Volumes of 2·0, 1·5, 1·0 and 0·5 millilitres are measured into labelled hard glass test tubes, and the alcohol is evaporated off by heating in a boiling water bath. To each tube is added 0·15 millilitre of absolute alcohol, 0·20 millilitre of freshly prepared 2% m-dinitrobenzene solution in methanol and 0·20 millilitre 15% potassium hydroxide solution in methanol. After thorough mixing of the ingredients, the tubes are placed in a water bath at 25° C. in the dark for seventy-five minutes. Each tube is then diluted to seven millilitres with absolute alcohol and compared with the standard cobalt chloride solution previously described. The solution with colour most like that of the cobalt chloride is selected for the quantitative comparison in the colorimeter. A green glass screen is inserted above the source of illumination in the colorimeter to eliminate interfering yellow and brown coloration.

It has already been stated that the cobalt chloride solution compares satisfactorily with that developed by treating 0·5 millilitre of 0·01% androsterone solution with the colour developing reagents. In the test, the ratio for the standard to the unknown multiplied by the factor 0·057 gives the number of milligrammes of 17-ketosteroids in the volume of alcoholic extract used. The formula

$$\frac{\text{standard}}{\text{unknown}} \times 0{\cdot}057 \times \frac{5}{\text{volume of alcoholic extract used}} \times 10$$

gives the number of milligrammes of 17-ketosteroids in the twenty-four-hour collection of urine.

Discussion.

The reasons which led us to modify the Drekter method for estimating 17-ketosteroids in urine are as follows.

Firstly, the intensity of colour, as well as the volume of solution produced in the Drekter technique, was found to be inadequate for use in a Klett visual colorimeter. An amount of 0·5 to 1·0 millilitre of the final extract in the Dingemanse method (corresponding to approximately 30 to 60 millilitres of urine when the volume of the twenty-four-hour collection was of the order of 1500 millilitres) was necessary to provide a suitable intensity of colour and

sufficient volume for use in the Klett colorimeter. In the Drekter method the colour was developed by extraction of only one millilitre of urine. Further, it is convenient to develop colour with the residue from several different volumes of the alcoholic extract containing the 17-keto-steroids, for example, 0·25, 0·5, 0·75 and 1·0 millilitre, so that one comparable with the colour of the standard solution can be selected for the quantitative estimation in the colorimeter. In order to meet these requirements we have extracted ten to twenty times the volume of urine suggested by Drekter and his co-workers.

Because of the larger volume of urine processed, we have preferred to make three extractions with ether, which is then washed twice with sodium hydroxide and finally with distilled water until the sodium hydroxide is completely removed, rather than to use the Drekter technique, in which there are only one ether extraction, one washing with sodium hydroxide solution and one with distilled water. Even the former procedure greatly reduces the time required to extract and purify the 17-ketosteroids from urine by the Dingemanse technique. It also ensures complete extraction from the larger volume of urine treated, as well as adequate removal of interfering substances.

Methanol has been substituted for ethanol as solvent for the m-dinitro-benzene and potassium hydroxide in the colour-developing reagents. The potassium hydroxide solution in methanol remains free from the opalescence caused by deposition of carbonate and can be used for some months, but it is still necessary to use freshly prepared m-dinitro-benzene reagent.

The substitution of cobalt chloride solution for the colour developed in a standard solution of androsterone has proved very satisfactory and overcomes the difficulty in obtaining pure crystalline androsterone for this purpose. If a green glass screen is inserted between the source of illumination and the colorimeter cups containing the solutions, the comparison of standard and unknown can be made satisfactorily in a visual colorimeter in a dark room.

Urinary pigments appear to be less soluble in ether than in extractants, such as benzene and carbon tetrachloride, previously used, since we have not found it necessary to treat the final alcoholic extract with animal charcoal to remove urinary pigments since adopting the ether extraction method.

Conclusion.

This modification of the Drekter method offers a simple means of making an accurate assay of 17-ketosteroids in a reasonable time and without elaborate equipment. It is an improvement on the older method of Dingemanse, because only one-tenth of the total twenty-four-hour secretion of urine needs to be assayed, and the tedious repeated extraction with several solvents is eliminated. It is more satisfactory than the original Drekter method for those using the ordinary type of visual colorimeter, and it covers a range of possible concentrations of 17-keto-steroids in the specimen being investigated. With the original Drekter method repetition of the whole extraction and estimation would be necessary for those specimens in which the amount of 17-ketosteroids happened to be outside rather restricted limits.

Summary.

1. The Dingemanse method for extraction and estimation of 17-ketosteroids is briefly summarized.

2. The rapid micro method of Drekter *et alii* is also summarized.

3. Modification of the Drekter method is described. In this method an artificial colour standard is substituted for the pure androsterone standard used in estimations of 17-ketosteroids. A visual colorimeter can be used for the final estimation.

Acknowledgements.

I am greatly indebted to Mr. H. Holden, of the Walter and Eliza Hall Institute of Medical Research, Melbourne, for his help in developing the cobalt chloride solution to replace the androsterone standard solution.

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A REVIEW OF SHARK ATTACKS IN AUSTRALIAN WATERS SINCE 1919.[1]

By V. M. COPPLESON,
Sydney.

. . . the dragon that is in the sea.
—ISAIAH XXVII : 1.

FROM Australia's earliest history, sharks have been known in her waters. In 1623 the Dutch navigator Carstenzoon recorded the presence of "sharks, sword-fishes and the like unnatural monsters" near Cape York. William Dampier in 1699 sailed the *Roebuck*, the first British naval ship to visit Australia, into a Western Australian bay which he named "Shark's Bay".

The first account of an attack by a shark in Australian waters was written in 1793 by Tench in "The Narrative of the Expedition to Botany Bay". He refers to a female aboriginal, who was bitten in two in New South Wales about 1790. François Péron, who accompanied Baudin's expedition, described an attack by a shark at Faure Island, Hamelin Harbour, Western Australia, in March, 1803. Sharks were apparently feared by the early settlers, and in *The Sydney Gazette* of July 20, 1806, there is a "caution to parents", warning them that a shark was hovering round Hospital Wharf.

Since these times, with increased population, the popularity of surf bathing and the advent of pearl diving, shark attacks have become more numerous. Each year about four or five attacks occur on the coast of Australia, of which about two or three are on pearl divers. A detailed list of shark attacks up to 1933 was published in this journal, and it is proposed shortly to publish a further detailed list to 1950. This paper briefly reviews the attacks on swimmers or persons bathing since January, 1919. There were 77 such attacks, of which 42 occurred in the surf and 31 in harbours, rivers or estuaries, whilst four were on swimmers in the open sea or at long distances from the shore (Figure I). There have been excluded 33 attacks on pearl divers (between 1926 and 1936), and several attacks at Darwin and along the north coast of Australia.

Injuries to Fishermen.

The numerous reports of injuries to fishermen, one of which was fatal, show that all's not fish that cometh to the net. These also have been excluded, and also reports of swimmers who have disappeared. Such disappearances are often credited to shark attacks without any evidence. In one instance a naval petty officer, who was reported to have been taken by a shark in Melbourne, was found next day at Albury, 200 miles away.

Mutilation of Dead Bodies.

Amongst the incidents recorded are a number of reports of the mutilation of dead bodies by sharks and of the finding of human remains in captured sharks. It was

[1] Read at a meeting of the Section of Surgery, Australasian Medical Congress (British Medical Association), Seventh Session, Brisbane, May-June, 1950.

once held that sharks did not attack dead bodies. There is ample evidence to show that this view is not correct.

It is often stated that sharks have great powers of digestion. Judged by mammalian standards, this is not so. There is little analogy between the physiology of digestion in sharks and that of mammals. The gastric juice of sharks contains little, if any, hydrochloric acid. From mouth to anus, the alimentary canal of a ten-foot shark would not measure more than eight feet.

The discovery of human remains in sharks' stomachs is not infrequent. In five or six cases, a human limb with little sign of digestion has been found on the opening of a shark, in which it had evidently been present for a week or more. In the "shark-arm" case, the arm had apparently been in the shark's stomach for several weeks. It was in a good state of preservation with only minor signs of digestion.

has been credited with similar attacks. It is thought that this shark may be responsible for the attacks on boats in Victoria and South Australia. So far, no identification has been reported.

Analysis of Details of Attacks.

An analysis of the details of the attacks since 1933 shows that they agree in the main with the findings of the previous paper.

Attacks are most common between the months of November and April, particularly in the warmer weather (Figure II). South of Mackay, Queensland (latitude 20° south), in 63 recorded instances, only one attack has fallen outside the period from October 20 to April 20. This, curiously enough, was the most southerly of all. It took place at Flinders Island, Bass Strait, on August 18, 1949. In the Sydney and Newcastle areas, all except one of 40

FIGURE I.
Showing location of shark attacks since 1919.

In a recent shark attack at Broome, Western Australia, a young woman lost her left arm. Eight days later the shark was caught. When its stomach was opened, the arm was found. The ring which was on one of the fingers the victim now wears on her right hand.

Numerous attacks on boats and rowing skiffs have also been recorded. In one instance three men lost their lives when their boat was attacked, and one man lost his life in another attack. The evidence against the sharks responsible literally comes out of their mouths. Some teeth are usually left in the woodwork of the boat by which their identity can be established. In every case in Australia, such teeth have been those of the blue pointer (mako). In other parts of the world, the white shark

attacks have occurred between December 14 and April 14. North of Mackay attacks have been reported in all months of the year.

Most of the attacks occur in the afternoon, usually between 3 and 6 p.m. (Figure III), and many take place close to the shore in very shallow water. Attacks have been recorded at all distances (see Table I) and at most depths (Table II). Those in a crowd have been taken as well as the "shark-baiter" (Table III). However, it is usually the lone bather or one of a small group or on the edge of a crowd, or a "shark-baiter" several hundred yards out, who is singled out. It is a common story that a number of men were out a long distance waiting for a "shoot", which they all took except one, who was then

attacked by a shark. Attacks have taken place in all sorts of weather, on dull days and fine days, at high tide, medium tide and low tide, in clear water and muddy water and even in brackish water. At times there has been a sandbank with an inshore channel. Most surfers believe that attacks are more likely in calm water, but they are as frequent when there are good "shoots" and heavy surf.

Usually only one bather is attacked, and there has been only one definite instance in which two persons have been injured by bites in the same attack. This was at Coolangatta in October, 1937. It is not certain whether one or two sharks were involved. At Maria River, in 1937, four brothers were bathing. Two of them were injured; one was bitten by a shark, the other was undoubtedly injured by the shark's fin. In a recent attack at Cairns, a bather was similarly injured, though only slightly. The shark often makes two or three attacks, which are usually confined to the victim even though others may be near by. In the majority of cases, the victim reaches shore unaided or is rescued. Great heroism has been shown by surfers and members of surf life-saving clubs in swift and daring rescue of their comrades. There had been no instance of a rescuer being attacked, except perhaps in the Coolangatta case, in which the second man was swimming in deep water close to the first victim at the time and was swimming towards him when attacked.

TABLE I.

Shark Attacks (41) Relative to Distance from Shore.

Distance. (Yards.)	Number of Attacks.
0 to 10	11
10 to 50	14
50 to 100	5
100 to 600	11

TABLE II.

Depth of Water in 27 Recorded Attacks.

Depth of Water.	Number of Attacks.
Shallow, depth unknown	2
2 feet	2
3 feet	6
4 feet, or waist deep	10
5 feet	2
Deep, but depth unknown	2
12 to 20 feet	3

Wounds and Mortality Rate.

Sharks may attack with great force and ferocity. Wounds may be caused by the shark's bite, by its fins or by the impact of its rough hide. Wounds due to the bite may be amputation of limbs or deep lacerations, usually with loss of tissue in the limbs or trunk, which may open the thoracic or abdominal cavities. Bones like the femur may be bitten through cleanly. The first attack is usually on the legs or buttocks. It is common for the victim to have one or both arms snapped off whilst trying to fend off the shark. Straight lacerations and wounds may be due to the shark's fins, whilst the multiple skin abrasions, usually arranged in definite rows and generally described as "tooth marks", are due to the impact of the shark's rough hide. The small wounds in some cases may be caused by small sharks or other fish.

TABLE III.

Shark Attacks (25) Relative to Number Bathing.

Number of Persons.	Number of Attacks.
Bathing alone	5
Under 10	10
Less than 20	3
30	2
Between 30 and 40	2
40 to 70	1
Several hundred	2

Of the attacks on bathers, the result in four is not known; of the remainder of the victims, 51 died (one double attack) and 23 recovered. Of the 51 who died, all but seven were brought ashore, and 25 died during rescue or before being admitted to hospital. Thirty-one were admitted to hospital, 17 of whom died after admission. In a number of the recorded instances only minor injuries were inflicted, and in several it is doubtful whether sharks were responsible. Where there is a definite bite by a shark, the mortality rate has been about 80% or more. The mortality rate among native divers is very much lower. Prompt rescue and first aid probably explain this.

Man-Eating Sharks.

There are about 35 species of sharks found along the coast of New South Wales, and many more in other parts of Australia. Gilbert Whitley, the ichthyologist of the Australian Museum, regards the sharks along the eastern coast of Australia as living fossils—the almost unchanged remnants of the marine fauna of a prehistoric sea, which existed to the east of Australia in the Eocene period.

At least six Australian sharks have been regarded as dangerous to man (Figure IV). They are: the tiger shark (*Galeocerdo cuvier*), the whaler shark (*Galeolamna*

TABLE IV.

Details of Sharks Caught by Meshing.

Period.	Whaler.	Tiger.	Grey Nurse.	Blue Pointer.	Hammer-head.	White.	Not Classified.	Total.
December 1, 1939, to December 1, 1940	76	62	141	81	62	113	216	751
December 2, 1940, to December 1, 1941	109	80	185	120	71	16	124	705
Three Year Period, May, 1947, to April, 1950.								
May, 1947, to December, 1947	23	15	18	66	46	—	(a)	168
December, 1947, to December, 1948	79	67	27	24	63	—	(a)	260
December, 1948, to December, 1949	79	7	13	4	5	—	(a)	108
December, 1949, to April, 1950	15	1	0	0	5	—	(a)	21
Total since May, 1947	196	90	58	94	110	—	494	557

(a) During this peirod, 494 unclassified sharks caught.

macrurus), the blue pointer or mako (*Isuropsis mako*), the hammerhead (*Sphyrna lewini*), the grey nurse (*Carcharias arenarius*) and the white shark or white pointer (*Carcharodon albimors*).

It was once thought that the grey nurse was responsible for most attacks. This shark chases its prey in the open sea. There is little evidence to support its evil reputation, although the wounds in a few instances may have been caused by the teeth of a shark such as the grey nurse

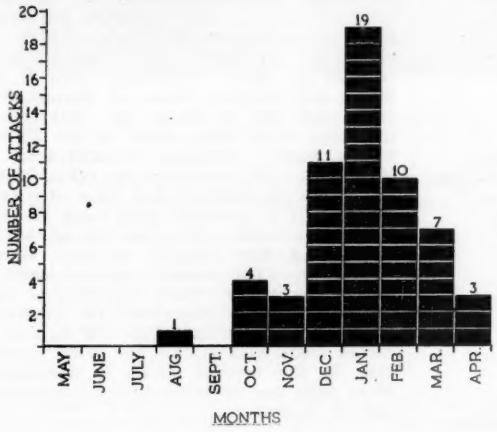

FIGURE II.
Showing the month of attack on 58 recorded occasions.

or possibly the blue pointer. The blue pointer or mako is also a pelagic shark. There is no evidence yet to incriminate it as a man-eater. It is known to be responsible for attacks on boats and probably surf skis on the eastern coast. Hammerhead sharks have been known to attack man in other parts of the world, but there is at present no evidence against the Australian hammerhead. It is a distinctive shark and easily recognized at a distance. The fact that it has never been reported or seen during an attack suggests that it has been responsible for few if any attacks. The white shark is the shark which follows ships. It is undoubtedly a savage shark and must be regarded as a man-eater. This shark is probably

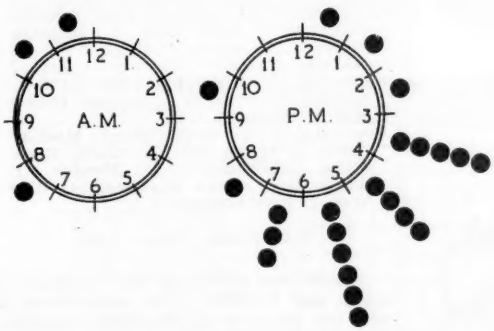

FIGURE III.
Showing the time of attack on 28 recorded occasions.

responsible for attacks on boats and possibly on bathers on the southern coast of Victoria and South Australia. The whaler and the tiger sharks are proved man-eaters. The evidence implicating them is complete. The whaler is the scavenger shark usually responsible for the attacks in bays, harbours, creeks and estuaries and around the mouths of harbours. It basks in warm shallows and even enters fresh water. The tiger shark is responsible for most of the outside shark fatalities. Dr. J. Nimmo has informed me that the divers of the Barrier Reef regard any shark over six feet in length as a man-eater and disregard any under this size. They consider the tiger as the most vicious of the sharks. The teeth of each of these sharks are distinctive. This is the easiest means of distinguishing them. (Figure V).

TABLE V.

Details of Beaches at which Sharks were Caught by Meshing between January 14, 1946, and October 12, 1947.[1]

Site.	Whaler.	Tiger.	Grey Nurse.	Blue Pointer.
Palm Beach	4	20	11	5
Whale Beach	2	11	11	4
Avalon	3	2	3	2
Newport	3	7	2	2
Mona Vale	1	2	0	1
Narrabeen	4	22	12	5
South Narrabeen	—	—	—	—
Collaroy	—	—	—	—
Dee Why	0	2	6	1
Curl Curl	0	5	9	2
Harbord	4	3	3	2
Queenscliff	2	1	1	5
North Steyne	—	—	—	—
Manly	3	8	8	6
Bondi	7	8	4	8
Tamarama	—	—	—	—
Bronte	3	5	1	2
Coogee	0	2	3	3
Maroubra	1	8	1	3
North Cronulla	—	—	—	—
Cronulla	3	7	4	2

[1] One blue pointer was caught on January 9, 1947, and no more were caught until the fortnight beginning April 28, 1947, when four were caught; then no more were caught until June 23, 1937, after which there was a fairly consistent catch. No tiger or grey nurse sharks were caught between July 7 and October 12, 1947, except one tiger on July 11; no tiger sharks were caught for four months from August 4 to December 8, 1946. No whalers were caught between January 6 and February 28, or between September 1 and October 28; then there was a fairly consistent catch, although low in numbers throughout. However, 110 were caught between December 16, 1946, and July 11, 1947, 49 of which were caught in the five weeks from December 23, 1946, to February 2, 1947.

Shark Meshing.

Numerous ingenious methods have been suggested to eliminate the danger of shark attacks and to protect bathers. At the instance of the Surf Life Saving Association, the Government of New South Wales, after a

TABLE VI.

Sharks Caught, Summer and Winter.[1]

Year.	Winter (June to September).	Summer (October to May).
1938	53	465
1939	32	148

[1] Similar figures were recorded in later years, but the difference was not so pronounced.

series of fatal attacks in the State, appointed in 1934 a Shark Menace Advisory Committee under the chairmanship of Mr. (now Judge) Adrian Curlewis, to investigate methods of securing the protection of bathers from shark attack. After taking evidence and considering the matter exhaustively, they recommended to the Government that shark meshing should be introduced on the beaches around Sydney. Meshing consists of laying a long twine or rope net overnight near a beach and removing it by a trawler in the morning. It is to the credit of the Government of New South Wales that, in spite of strong criticism that the proposal was "a stupid, futile waste of money", it was willing to adopt unusual methods to meet an unusual foe. The experiment appears to have been well worth while. Meshing was begun in 1937. From this date, thirteen years ago, not one attack by a shark has occurred on any ocean beach in the area meshed (Figure IX). In the

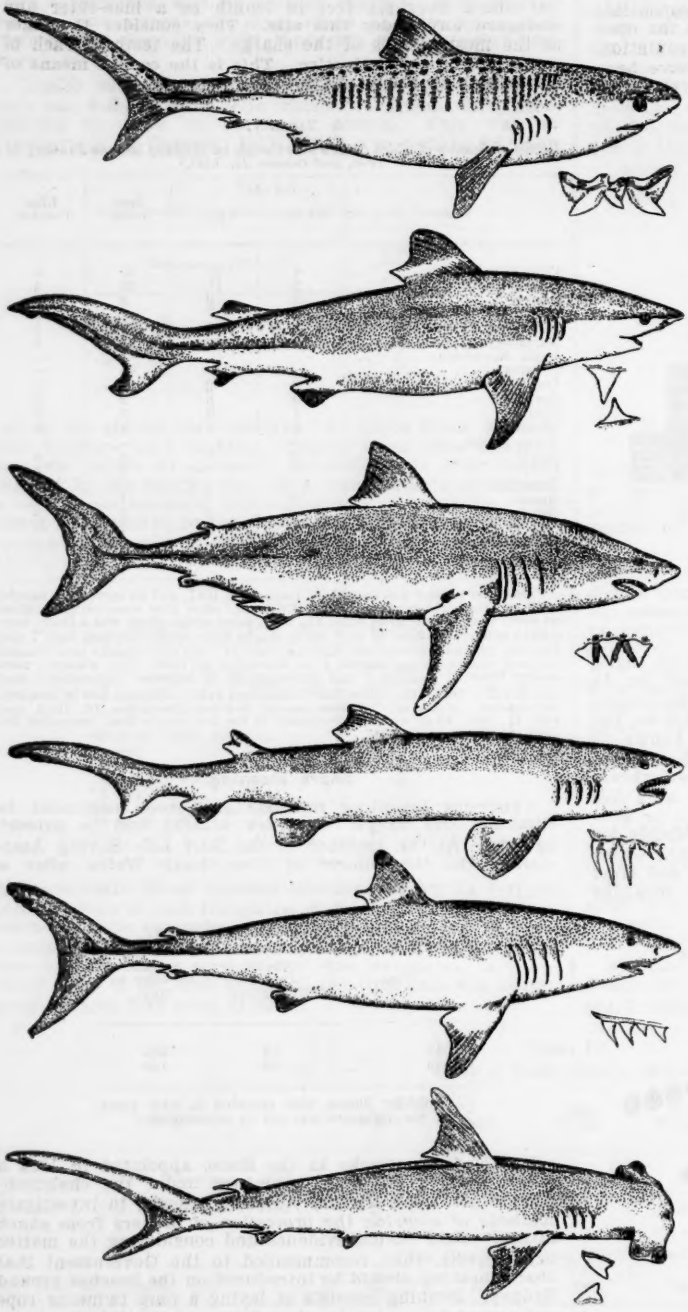

FIGURE IV.

The commonly suspected man-eating sharks, from above downwards, as follows: (i) the tiger shark (*Galeocerdo cuvier*); (ii) the whaler shark (*Galeolamna macrurus*); (iii) the white shark (*Carcharodon albimors*); (iv) the grey nurse (*Carcharias arenarius*); (v) the blue pointer (*Isuropsis mako*); (vi) the hammer-headed shark (*Sphyrna lewini*). The teeth of each species are shown behind the head of the corresponding shark.

previous thirteen years, 13 attacks had taken place on these beaches. The longest interval between attacks was one of five years from 1929 to 1934. Attacks which occurred during this period were confined to harbour and river waters where there had been no meshing.

I am indebted to Mr. C. Mack, who was secretary of the Shark Menace Advisory Committee, for the following information concerning the results of meshing. The first contract was let with Cranwick Fisheries, Limited, and started in October, 1937; 517 sharks of all species were caught until October 28, 1939. Contracts with C. R. Stuart and Company began on December 2, 1939, and ran to March 23, 1941, when the ships were taken over by the United States Navy. Meshing recommenced in May, 1947. The accompanying table (Table IV) shows the numbers and types of sharks caught. It is probable that these are not strictly accurate. The beaches at which the sharks were caught are also shown (Table V). The smaller numbers meshed during the winter (Table VI) suggest that these sharks go elsewhere or hibernate during these months. The low figures in recent years suggest that the shark population in the meshed areas is decreasing. More data are required before conclusions can be drawn.

The Location of Attacks.

Of the 77 attacks on bathers and swimmers since 1919, all except nine have occurred in New South Wales or Queensland (Table VII). The most southern attack was at Flinders Island in Bass Strait in October, 1949. No authentic attack is known to have occurred south of latitude 40° or in Tasmania.

Analysis of New South Wales Attacks, 1919 to 1949.

Sydney Harbour: Middle Harbour 2, Sirius Cove 1, White Bay 1, Camellia 1	5
Sydney beaches: Coogee 3, Bondi 3, Maroubra 2, Bronte 1, North Narrabeen 1, Dee Why 1, Queenscliff 1, North Steyne 1, South Steyne 1, Collaroy 1	15
Botany Bay and George's River: North Brighton 2, East Hills 1, Milperra Bridge 1, Kentucky 1, Como 1	6
Newcastle Harbour: Throsby Creek 2	2
Newcastle Beaches: Stockton 3, Newcastle 2, Merewether 1, Bar and Cook's Hill 3, Redhead 1	10
Elsewhere in New South Wales: Macleay River 1, Byron Bay 1, Maria River (Port Macquarie) 1, Forster 1, Austinmer 1, Lake Macquarie 1, Woy Woy 1, Port Hacking 1	8
New South Wales total	46

Attacks are extremely rare in South Australia and Victoria. The reason that they are not common in Western Australia is probably that those who expose themselves to the risk there are few. The numbers of attacks in these States since 1919 are: Western Australia four, South Australia two, Victoria two. Only three attacks have been recorded in the history of South Australia. In Victoria the last attack on a bather occurred in 1930; the only fatal attack prior to this was at Albert Park in 1876. The details of the attacks in Queensland are shown in the following summary:

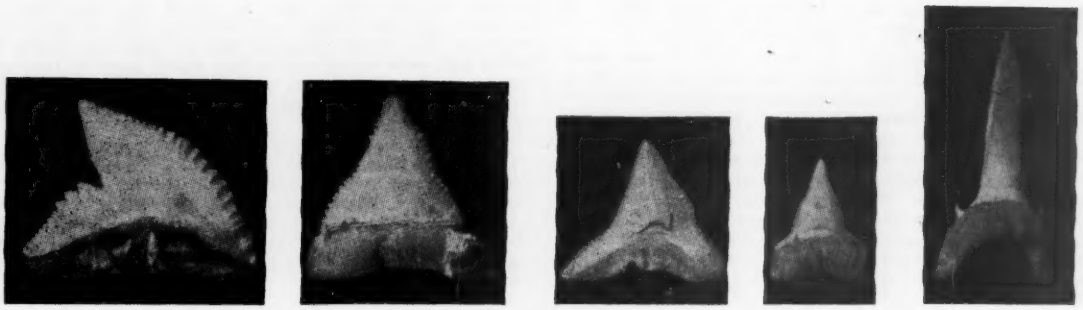

FIGURE V.

Isolated teeth of sharks: (*a*) the tiger shark; (*b*) the white shark; (*c*) the whaler, upper jaw; (*d*) the whaler, lower jaw; (*e*) the grey nurse.

Analysis of Queensland Attacks, 1919 to 1949.

Cairns: Trinity Beach 3, Ellis Beach 2, Yorkies Knob Beach 1	6
Townsville: Ross Creek 5, Cleveland Bay 1, Magnetic Island 1, Kissing Point 1	8
Elsewhere in Queensland: Mackay 1, Yepoon 1, Paliba 1, Caloundra 1, Bulimba (two involved) 1, Coolangatta (two deaths) 1, Southport 1, Currumbin 1	8
Queensland total	22

Examination of the location and dates of attack gives some suggestive information. Apart from attacks on pearl divers along the Barrier Reef, it is obvious that the majority of attacks occur in harbours and estuaries and on beaches near the entrances. More than half the attacks on bathers and swimmers have occurred in the vicinity of Sydney, Newcastle, Townsville and Cairns. The yearly freedom from attack along the New South Wales coast from April to December is supported by the meshing figures given above, and by evidence of the feeding habits of captive sharks. There is also reason to believe that at least along the east coast, the dangerous sharks which are cold-blooded creatures are active only when the sea temperature is about 70° F. or higher.

If the attacks in given areas are studied, a most striking feature is the occurrence of many of the attacks in sets or sequences. Examples of several attacks in one area over a short period have been reported. On August 8, 1899, three shark attacks occurred at Port Said in the same vicinity. Between July 6 and July 12, 1916, on the bathing beaches of New Jersey in Sandy Hook Bay at the mouth of New York Harbour, four bathing fatalities took place which were ascribed to a white shark. In New Guinea, early in 1931, attacks occurred in the same vicinity on three successive days.

Somewhat similar sequences are apparent in Australian attacks; this will be seen from the following summary:

Attacks in a Given Vicinity at Short Intervals, New South Wales Only.

Coogee: February 6, 1922; March 3, 1922; Bronte, February 30, 1924; Coogee, March 27, 1925.

Bondi: April 14, 1928; January 12, 1929; February 8, 1929.

Queenscliff, Manly, January 7, 1934; Dee Why, March 13, 1934; North Steyne, April 1, 1934; North Narrabeen, March 2, 1935; South Steyne, Manly, February 4, 1936.

George's River: East Hills, January 29, 1934; Milperra Bridge, December 31, 1934; Kentucky, December 31, 1934.

North Brighton: January 23, 1940; February 4, 1940.

Middle Harbour: January 6, 1942; December 26, 1942.

Stockton Beach, Newcastle, February 12, 1948; Bar Beach, Newcastle, January 26, 1949.

1. At Coogee Beach, Sydney, an attack took place on February 6, 1922; there was another attack on March 3, 1922, an attack on February 13, 1924, at Bronte Beach about two miles north, and a further attack at Coogee on March 27, 1925. There had not been a previous attack at Coogee, nor has there been any attack since those dates.

2. At Bondi Beach an attack took place on April 14, 1928, a further attack on January 12, 1929, another on February 8, 1929, and one at Maroubra, some six miles south, on February 18, 1929. There had been no previous

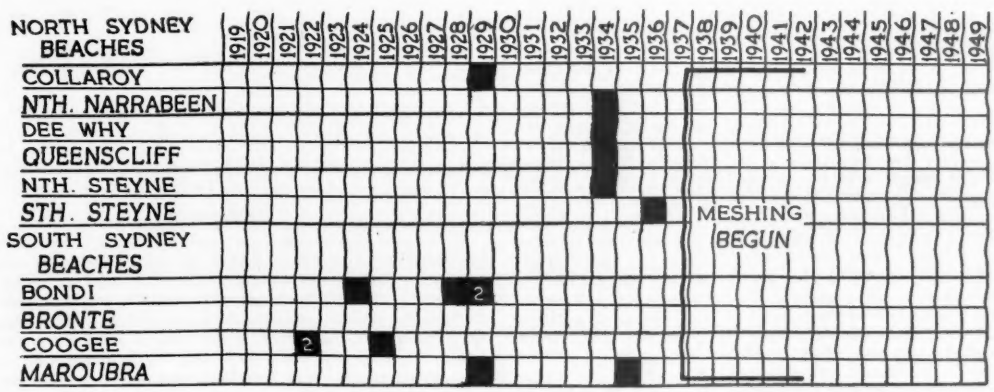

FIGURE VI.

Showing the effect of meshing. Each black square represents one shark attack, except where two attacks are shown by the figure 2.

attacks at Bondi, and there have been none since. A further attack took place at Maroubra in 1935.

3. An attack took place at Queenscliff Beach, near Manly, on January 7, 1934, one took place at Dee Why Beach, four miles to the north, on March 13, 1934; on April 2, 1934, there was an attack at North Steyne, just south of Queenscliff. On March 4, 1935, there was an attack at North Narrabeen, about seven miles to the north, and on February 4, 1936, one at South Steyne. The attacks were over a distance of about seven miles. No other attacks took place on any other Sydney beaches, nor was there anything to suggest a local increase in sharks. There had previously been no attack in this area, nor has there been one since.

TABLE VII.

Attacks on Swimmers and Bathers, 1919 to 1949.[1]

Place.	Number of Attacks.
Queensland	22
New South Wales	46
Victoria	2
South Australia	2
Western Australia	4
Bass Strait, Flinders Island ..	1
Total	77

[1] Thirty-three attacks on divers and several in Northern Territory excluded.

4. At George's River a man was killed by a shark at East Hills, twenty miles from Botany Bay, on January 27, 1934; another attack took place further up the river (one mile), near Milperra Bridge, at 4.30 p.m. on December 31, 1934. At 8.15 the same evening another attack took place three miles up the river at Kentucky.

5. At North Brighton, Sydney, a boy was killed by a shark on January 23, 1940; twelve days later, a quarter of a mile away, on February 4, 1940, a man was killed by a shark.

6. At Egg Rock, Bantry Bay, Middle Harbour, Sydney, a young woman lost her life in a shark attack on January 6, 1942; at Instone Point, Bantry Bay, a short distance from the previous attack, another young woman lost her life by shark attack on December 26, 1942.

This grouping is not confined to Sydney. Five attacks in the vicinity of Cairns are in two groups (Figure VII). Three attacks occurred in the first group: one at Trinity Beach on June 19, 1945, a second one at Trinity Beach on April 19, 1946, and the third at Ellis Beach, a few miles south, on August 19, 1946. The second group consists of two attacks, one at Ellis Beach on April 18, 1949, the other at Yorkey's Beach, some miles south, on August 29, 1949.

Sharks of types known or reputed to be man-eaters are caught with great frequency in the vicinity of beaches where large numbers of people are constantly bathing. There can be little support for the view that the sea is full of man-eating sharks hunting in packs, ready to pounce on unwary bathers. In all the Australian attacks, except one, if there has been any evidence, it has been that only one shark was concerned in the attack, and in the majority of cases the shark is seen. The evidence, which includes the freedom from attacks over long periods, the continued presence of man-eating sharks, the attacks in sequence, and cessation of attacks once a particular shark is caught, suggests the guilt, not of many sharks, but of one shark. It suggests the presence of a vicious shark which patrols a certain area of the coast, of a river or of a harbour, for long periods. If it leaves—and there is evidence to suggest that it either leaves its area or hibernates for a time each year—it returns to the same patrol and may do so for a number of years. The extent of its territory appears to be about ten to twelve miles. Its presence is usually disclosed by its viciousness. Dogs may be attacked, fish taken from lines, and in other ways it may disclose itself. Once an attack has taken place at a given spot the danger still remains, and it must be a warning that further attacks may be expected within ten miles and even up to one or two years later in the same area, unless the shark is destroyed. In this respect the man-eating shark appears to be somewhat analogous to the man-eating tiger.

Based on this theory, a letter was written by me to *The Sydney Morning Herald* on January 24, 1940, the day after a boy had been attacked and killed at North Brighton Beach, Sydney, in which the possibility of a further attack near North Brighton Beach was predicted. Danger often comes quickly when it is despised. A further attack took place almost at the site of the previous attack twelve days later.

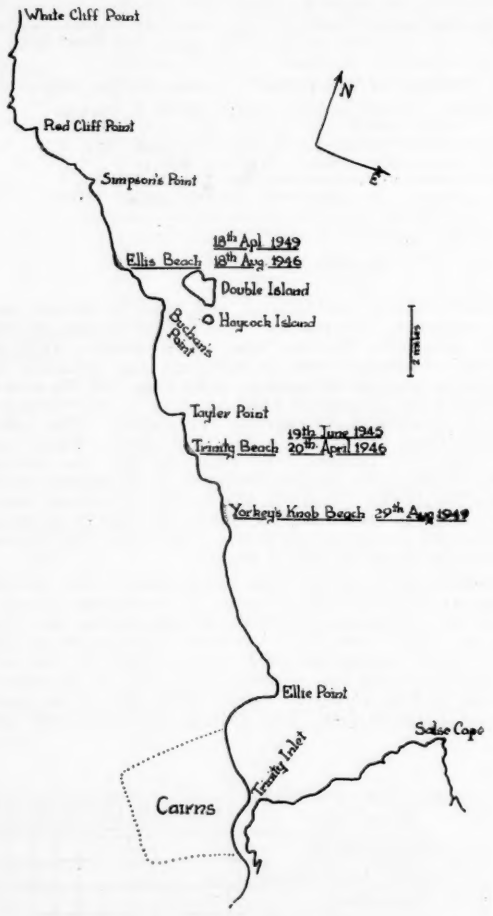

FIGURE VII.

Conclusion.

It would appear that in Australian waters there is an ever-present danger of shark attack, especially along the eastern coast north of Port Hacking and probably along the northern and north-western coasts, on beaches, and in harbours, creeks, rivers, and estuaries. The danger to any individual bather is infinitesimal and very much less than the risk of serious injury in a motor-car accident. Nevertheless, it is a horrible and fearful type of injury, which falls mainly on those who are full of life and youthful vigour. Precautions are necessary for safety. This can best be obtained by bathing in enclosed areas. However, meshing, which has been introduced by the New

South Wales State Government, appears to have eliminated or greatly reduced the risk of attack. Whilst the time during which meshing has been carried out is too short to come to definite conclusions, so far it appears to have proved successful, and the meshing returns appear to suggest a reduction in the shark population of the beaches.

A measure of prophylaxis may also be able to be taken when the presence of a dangerous shark is known in any vicinity. It should be the responsibility of local bodies to detect such sharks, and they should be able to call upon other authorities to assist them by meshing, by the provision of shark anglers and perhaps by other methods. Undoubtedly a number of fatalities could have been prevented if these facts had been known and the proper precautions taken.

Vigilance both before and after an attack on open beaches, in harbours or in inland waters should never be relaxed in the presence of a dangerous shark. Such a shark must be hunted until it is destroyed. In conclusion, it would seem that over the last twenty years we have made considerable progress in our knowledge of sharks and their habits in relation to attacks on man, and considerable advance in methods of protection against their attacks.

THERAPEUTIC DIAGNOSIS IN PÆDIATRICS.[1]

By ROBERT SOUTHBY, M.D., B.S., F.R.A.C.P.,
Melbourne.

SINCE the last meeting of Congress in Perth in 1948 there have been several happenings of extreme importance in the field of pædiatrics to which I consider special reference should be made on this occasion of the opening meeting of the Section of Pædiatrics.

Firstly, the Australian Pædiatric Association has just been inaugurated at a meeting held prior to the opening of Congress. This important move has been eagerly awaited by pædiatricians in this country for some time past, and the association began to take shape at the time of the Perth Congress, at which a small executive committee was appointed to work out some preliminary details. After several meetings had been held, plans gradually evolved, and the association has now been successfully launched. I am sure it has the best wishes of all interested in the study of pædiatrics for its future success.

The principal aims of the new body are as follows: to encourage the study of pædiatrics in Australia; to improve the standards of pædiatric practice and to stimulate research in pædiatrics; to act as a consultant and advisory body on child health generally; to promote personal contact and friendship among pædiatricians at home and abroad.

Membership is for those who are specializing in pædiatrics, or who are members of the staffs of hospitals caring for children. All such members shall be pædiatricians of at least five years' standing.

For the inauguration of the association there are 60 members, made up of 20 each from New South Wales and Victoria, seven each from Queensland and South Australia, and three each from Tasmania and Western Australia. It is proposed that the membership will be increased from time to time. It was the unanimous wish of the representatives from all States that Dr. H. Douglas Stephens should be the inaugural president, and I am sure that it was most gratifying to all concerned that Dr. Stephens has seen fit to honour us by accepting this position. It is generally felt by those who know him personally that he is truly a "Peter Pan" amongst pædiatricians in Australia. He never ages with the years, and it is an extremely good augury for the new association that it should have the advantage of his long experience and youthful enthusiasm to set it on its way.

Another important milestone has been the establishment by the Commonwealth Government of a Chair of Child Health at the University of Sydney, and it was with much gratification, I am sure, that we heard of the appointment of Dr. Lorimer Dods of Sydney to this important post. I am delighted to see Professor Dods with us today and now offer him our heartiest congratulations and our best wishes for success and prosperity in this new field, which I am sure will be of inestimable benefit to the health of the children of this Commonwealth.

Thirdly, it is a cause for some satisfaction that the faculties of medicine at the various universities are gradually realizing the importance of pædiatrics in the training of the medical undergraduate, and last year for the first time the University of Melbourne included a pædiatric question in the first medicine paper in the final examination and appointed two pædiatric physicians as examiners for this question. Recently the same faculty has approved of the extension of the period for attendance of students at the Children's Hospital from eight to twelve weeks.

Fourthly, a matter worthy of note and much thought is the work recently published in Adelaide in connexion with a research on pink disease. This offers an entirely new line of approach, and will doubtless arouse interest and stimulate further study in this all-important problem in pædiatrics in this country in particular.

With these introductory remarks I propose to deal now with the subject of my presidential address, "therapeutic diagnosis in pædiatrics", or alternatively if you prefer it, "diagnostic therapeutics".

At the outset I should like to emphasize that in these days, when the scientific and laboratory side of our work has loomed so large on the pædiatric horizon, we should be particularly careful to avoid neglecting or completely losing sight of the importance of the carefully ascertained medical history and the equally important thorough and systematic clinical examination, remembering always the enormous amount of information that can be acquired by astute and meticulous observation.

With little children and especially infants we are perforce driven to rely on the old advice: eyes first and most, hands next and little, tongue not at all, or last and least.

In this respect I should like to digress for one moment to pay tribute to some of my old clinical teachers, remembering particularly Dr. Konrad Hiller, Dr. H. Douglas Stephens, the late Sir Richard Stawell, and the late Dr. John W. Grieve. To all of them I owe a great debt of gratitude and to all of them I acknowledge with grateful thanks any achievement that may have come my way in the field of clinical medicine as being due in large measure to their guidance and untiring help in my early years of training.

The title of my address is self-explanatory. I wish to demonstrate how, in a series of well-established clinical conditions, a diagnosis can be arrived at by a carefully ascertained history and clinical examination without outside assistance from the more specialized departments, upon which there is too much tendency in recent years to depend for the last word in diagnosis and even in treatment.

Let us for example consider the following case history. The patient is a first baby, born at full time after an uneventful pregnancy and confinement and weighing nine pounds at birth. The time of the year is mid-January and there is a particularly hot spell of weather, the midwifery nursery is overcrowded, and the staff is in short numbers. The infant causes nobody any concern for his first forty-eight hours, but on the morning of his third day the nursery sister reports to the obstetrician on his visit that Baby X looks very ill and has a temperature of 106·2° F., a pulse rate of 150 per minute and a respiration rate of 56 per minute. A glance at the chart worries the obstetrician, who fears that the infant has contracted a sudden acute infection, and he is concerned as to whether the baby should be given sulphonamide or penicillin or both. Incidentally, the baby's weight has dropped to seven and three-quarter pounds. This is a fairly common fallacy, and in these days of chemotherapy it

[1] President's address, read at a meeting of the Section of Pædiatrics, Australasian Medical Congress (British Medical Association), Seventh Session, Brisbane, May-June, 1950.

would seem to be a logical sequence to give such an infant possibly sulphadiazine at once. As you all realize, this would be the worst possible measure for this baby, who is obviously presenting the classical picture of dehydration fever of the newborn. All that he requires is that it should be somebody's particular job to see that he is given ample boiled water at frequent intervals during the next twenty-four hours. The result is dramatic, and the simple therapy confirms the correctness of the original diagnosis.

Another common problem is that of persistent vomiting commencing in an infant a few weeks of age. The vomiting occurs after each feeding once it has become established and appears to increase in quantity, and on occasions the mother ascribes what is suggestive of a projectile character to the vomiting. The first worry is that the baby may be developing a condition of pyloric stenosis, and he is observed after one or two feedings. This raises a doubt as to the presence of peristaltic waves, and it is also questionable whether a tumour is palpable. Doubtless you have all been presented with this query on a number of occasions. Further questioning reveals the fact that the baby is having a bowel action each day but that the motion is less in amount than previously, and in addition there has been either no loss or possibly a slight gain in weight. These latter facts rather discount true stenosis, but the vomiting persists, and wherever the facilities are available an opaque meal examination is usually made. The radiologist reports no actual stenosis and interprets his findings as being consistent with pyloric spasm. The interesting point in these cases is that often when the mother comes back with the infant to hear the radiologist's report and you inquire about the baby, her reply is in these words: "That was wonderful X-ray treatment, doctor—he has not vomited once since he was X-rayed." I am sure that you must all have had that experience. The lesson, I think, is this (and it is usually what I tell students now), that under such circumstances, and especially if X-ray facilities are not readily available, the baby should be given one drachm of pure barium sulphate with one feeding, and if the vomiting subsides then the condition is one of spasm and not true stenosis. Once again the therapy confirms the diagnosis between intermittent obstruction due to spasm and almost complete obstruction due to stenosis.

Yet another worrying type of infant is the one aged, say, eleven months, who was breast fed for only five weeks, after which artificial feeding became necessary. At this time the baby was given some orange juice, but did not like it very much, and so the mother did not persist with its administration. The baby progressed for about six months quite satisfactorily, but for the past eight weeks or more he has been somewhat irritable, not so keen on his food and not sleeping at night. For the past week before the doctor is consulted he has been very miserable, whining most of the night and disturbing the household constantly. On examination it is noticed amongst other things that the gums are swollen and somewhat reddened, and the mother's suggestion that it is "teething trouble" is a very easy trap for the unwary. The next possibility is that the infant may be going to declare himself as suffering from pink disease; but he is not photophobic or atonic, nor is he sweating or showing any rash or red cold hands and feet. A closer inspection reveals that the gums are injected and may tend to bleed on pressure and that the baby is much more restless and apparently in pain when he is handled, especially about the limbs. Microscopic examination of a specimen of urine reveals a condition of hæmaturia. The sickness is thus proved to be scurvy and the pronounced change in the clinical condition even in twenty-four hours with intensive ascorbic acid therapy will immediately clinch the diagnosis.

There are doubtless numerous cases of subclinical scurvy. If the history is carefully elicited and the baby thoroughly examined, and if the suspicion of vitamin *C* deficiency is aroused in the physician's mind, then it will be found that 50 milligrammes of ascorbic acid given three times daily are a much more efficient sedative than large doses of phenobarbital, bromides or acetylsalicylic acid. Once again the therapy has confirmed the diagnosis.

Still dealing with infants, let me refer to the problem of the baby aged perhaps nine or ten months who, according to the mother's story, has been troubled with constipation since birth and has always needed some laxative such as milk of magnesia, paraffin oil, "Agarol", syrup of senna or even small doses of cascara, and in spite of all these it is often necessary to use a soap pencil or a glycerin suppository or even a small enema of olive oil or soap and water. These babies appear to be well on general clinical examination and present no evident signs of any endocrine disturbance. Nevertheless, such infants will often respond dramatically to small doses of thyreoid extract given at regular intervals. I am sure that there are numbers of infants in whom the only manifestation of thyreoid deficiency is persistent and obstinate constipation. If this possibility is constantly borne in mind, then the appropriate therapy with thyreoid tablets will confirm the diagnosis beyond all doubt. If further confirmation of the basis of the trouble is needed, one has only to stop the thyreoid administration for a few days and it will be found that the baby is again becoming obstinately constipated.

Another most interesting group is that large one comprising those children who present allergic manifestations in one or another form. Firstly, with the problem of asthma one feels more than ever that a detailed and carefully ascertained clinical history will often throw a flood of light upon possible causes. Take an illustrative example of the little girl, aged five years, who has been subject to attacks of cough with some noisy breathing for the last two years. Inquiry shows that the cough is always worse after she has gone to bed and is likely to disturb her at intervals throughout the night—incidentally interfering with the parents' rest also. Once she is up and dressed she begins rapidly to improve and is generally well throughout the day. There is no definite seasonal incidence, and as far as the mother can determine, no food factor can be incriminated. There is a strong family history of allergy in several generations. Assessing the whole story and the clinical findings, particularly in view of the fact that the pollens and the "ordinary colds" can be excluded by the absence of any special incidence in spring or summer or in the case of the latter in the winter, we are able to arrive at the surmise that there is something to which this child is sensitive associated with her bedding or bedroom. Further questioning elicits the fact that she has always slept on a horsehair mattress and up to two years ago always had a flock pillow. At this stage she was given a kapok pillow, and more detailed inquiry reveals that the mother is certain that the attacks commenced and that the new pillow was installed on the day of their return from a particular holiday. The attacks have been persistent ever since. Obviously the next move is to remove the kapok pillow from contact with this little girl. The physician is almost as excited as the mother when she reports a fortnight later that her daughter has not had a disturbed night from coughing since the second night after the kapok pillow was replaced by one filled with hygienic wool.

The final proof of the therapeutic diagnosis in this story is to give the little patient back her old kapok pillow, when the physician has the satisfaction of hearing over the telephone the next morning that the child "had one of her worst nights last night".

Digressing for a moment to speak of the cough which is most obstinately troublesome at night, almost always commencing when the child goes to bed and the head is rested upon the pillow, one is presented with the cough due to mechanical irritation rather than actual inflammatory processes in the lungs. Having started, this cough may persist for an hour or more at a time and cease only when the child falls asleep from sheer exhaustion, only to be wakened in perhaps half an hour for a further bout of this persistent, dry, irritating cough, which by this time has disturbed both parents. So the whole household before many nights is suffering from a severe lack of sleep. Careful examination, after the detailed nature of the cough has been elicited, reveals one of two well-recognized causes in these cases: (*a*) a long, lax, œdematous uvula, which can be seen literally "flopping"

about and irritating the posterior pharyngeal wall or impinging upon the tonsil on one or other side; (*b*) an acute sinus infection with a considerable amount of thick mucopus trickling down the back of the naso-pharynx and so causing much mechanical irritation. Once these two possibilities for this type of cough have been recognized and efficient treatment of the local condition has been instituted, it is nothing short of dramatic to note the manner in which the cough disappears. Thus the provisional diagnosis is confirmed by the treatment carried out.

Let us return now to the allergies. Almost identical case histories are met with from time to time in infants suffering from eczema. Doubtless many of you can recall having seen an infant, aged seven months, who has been troubled by severe and apparently intractable eczema, which careful history-taking shows to have been present since the baby was weaned at the age of five months on account of illness of the mother. Since that time the infant has been on a dried milk mixture and meticulous care has been taken to ensure that the baby has received all the necessary vitamins. Amongst the daily ration there is one tablespoonful of fresh orange juice which the mother has made certain has been given regularly. Further interrogation shows that the mother is positive that there was no skin trouble at all prior to the artificial feeding. There is still the possibility that the feeding itself or some of the other vitamin preparations may be the underlying cause. However, orange juice is readily omitted from the menu for a start, and the mother is more than gratified to be able to report that at the end of one week the baby's skin is quite free of rash and "just as good as when she was being entirely breast fed". A return to the orange juice for even forty-eight hours is accompanied by a return of the rash in all its intensity. Such a sequence of events leaves no doubt whatever that this baby will in future need her vitamin *C* in the form of ascorbic acid tablets.

A further representative of this allergic group is the eight-year-old boy, an only child, always "nervy" and "highly strung", who is subject to frequently occurring attacks of abdominal discomfort, nausea and vomiting, on account of which he is often sent home from school with a "bilious attack". Inquiry shows that the father's family has several members with hay fever and asthma, and that the mother is at present under the care of a psychiatric physician. Further questioning will sometimes indicate that at the onset the child has some frontal headache or perhaps describes some difficulty in seeing the blackboard at school, but this does not always follow. Such a background and such attacks always arouse the suspicion of migraine in a child. When this is explained to the mother, she announces with some little delight that her own doctor hold her that she was suffering from migraine, and that her own mother had also had similar severe attacks. The child is then given suitable nervous system sedatives, which are administered for some considerable time, and the attacks fairly quickly subside. It seems that the longer the interval between the attacks, the less likely they are to recur. However, should sedation be stopped too soon (and this is often the case, because the mother considers that her son is so much improved that the treatment is no longer necessary), there is quickly a return of the old attacks. This amply confirms the nature of the condition by its response to the appropriate treatment.

Whilst speaking of the allergies one may be permitted to refer to another entity in children which I consider is inseparably linked with them, and that is achlorhydria. In a recent monograph this has been emphasized, and it is held that certain groups of clinical manifestations can be recognized as being associated with a condition of achlorhydria in children.

Briefly, apart from the allergic group, the patients in which are almost without exception lacking in hydrochloric acid secretion, there are three classes of children whom one has now come to recognize as needing therapy with dilute hydrochloric acid: (*a*) the infant with the so-called "lienteric" type of diarrhœa; (*b*) the pale child sent home from school on account of "anæmia"; (*c*) the child apparently suffering from "ulcerative colitis". The dramatic response in all three classes when dilute hydrochloric acid is supplied in adequate amount is the final evidence as to the diagnosis. I have said "adequate amount" advisedly, since it is surprising how much is needed by many of these children before the clinical benefit becomes evident.

At the risk of this procession's becoming tiresome, I should like now to refer for a few moments to the condition of family periodic paralysis, which, as you know, is a rare disorder, but at the same time a fascinating one, on account of both the interesting clinical history and the really dramatic and specific response to potassium chloride therapy.

With a condition closely akin to this, but without any family history, I have seen from time to time children who have presented a vague history of malaise and lassitude in the early morning, which has gradually become so pronounced as to interfere with their ability to make a start at school until nearly the middle of the morning —and this quite apart from laziness or scheming to miss lessons, for which they are usually wrongly blamed and even punished undeservingly. Potassium chloride acts most dramatically on these little subjects, who for some reason have developed a deficiency of this particular element, sometimes temporarily and at others apparently permanently, in which latter case they require a basal maintenance dose to ensure normal health. This is a most intriguing example of a tentative diagnosis being confirmed by the appropriate therapy.

Another matter of interest is the number of children who are disabled from time to time on account of colicky abdominal pain which recurs at intervals of perhaps weeks or months, transient in character and often not associated with vomiting. A careful history and clinical examination fail to reveal any definite underlying basis for the attacks, and one is forced back reluctantly to suspect the appendix as the offender. In this respect I believe that there is a condition of recurring appendiceal colic in children, quite apart from recurring inflammatory attacks of true appendicitis. X-ray examination with an opaque meal will sometimes give positive evidence of a kinked appendix, or an unduly long and tortuous appendix, with perhaps an indication of the presence of a fæcolith. Negative evidence, such as the radiologist's report that he is unable to visualize the appendix on several attempts, is, I think, equally valuable; this occurrence is often due to congenital or acquired stenosis of the appendix at its base.

In these cases it is justifiable to advise removal of the appendix. It is extremely gratifying to the physician when the surgeon is able to demonstrate some definite mechanical basis for the repeated attacks of colic, and even more gratifying to the parents to find that the child has no further attacks after appendicectomy—surely, you will all agree, another instance of diagnostic therapeutics.

Drug idiosyncrasies offer another interesting puzzle in pædiatric practice. At not infrequent intervals one comes across a child who is presenting certain symptoms or signs which, on careful inquiry, are found to date almost from the beginning of treatment with a particular mixture or tablet. Perhaps the conditions most often seen are the instances in which a recognized sedative has been prescribed, such as phenobarbital, chloral hydrate or bromide, and in which it has not only failed to quieten the child but has even caused the reverse effect and appears to have stimulated the little patient unduly. On the other hand, the manifestation may be in the form of a rash or other skin lesion. After careful inquiry the whole position will clarify itself. On discontinuance of the offending "sedative", the child quickly settles down to his normal activities and remains well so long as he is kept religiously away from the particular pharmaceutical preparation which was the cause of his indisposition.

Another nightmare which has loomed large in our field in recent years is that of the "highly strung", alert child who presents as "the nervous type of difficult feeder"—the hyperkinetic child. Doubtless you have all met this little patient who never seems interested in food or to become normally hungry, and almost drives his mother to distraction at feeding times. I always regard him as the

product of the difficult times through which we have all lived in the last generation, always in "top gear" and everlastingly "chasing the clock". The parents of this young child have more often than not been living with the grandparents, sharing a home, or perhaps living in a very small flat on the third or fourth floor of a large block of flats. Children being brought up under these conditions frequently react by developing an intense resentment towards food, especially anything other than liquids. Yet they are extremely active physically and never tire. They appear to be very economical little engines, reminding one of the "baby car" which does 100 miles to the gallon of fuel. A thorough examination and clinical investigation reveal no indication of evident organic disease as a basis for this distressing condition. Having decided upon the correct diagnosis, we advise the mother that a complete change of environment or management by a children's trained nurse will be the best line of treatment. Alternatively (not that we would wish it deliberately), the onset of some acute illness in these children necessitating a trip into hospital and a complete change of environment will on most occasions effect a rapid cure. Thus is provided adequate confirmation of the provisional diagnosis by the response to the type of management recommended.

Conclusion.

I trust that I have not bored you with this presentation of a series of clinical entities, which I consider can be strongly suspected by careful (even meticulous) history-taking and clinical examination, the correctness of the diagnosis being confirmed as a result of the therapy instituted. Hence my excuse for the apparently anomalous title of "diagnostic therapeutics" (or alternatively "therapeutic diagnosis").

Should this contribution on my part be the means of focusing attention on the importance of the careful taking of a clinical history, on the conscientious physical examination and on correct assessment of the information thus obtained, then I shall feel that my efforts have not been in vain.

This is of all the more importance in these days when so many and varied aids to diagnosis are offered to us by our colleagues in the laboratory; but without wishing in the least to decry these methods, which are at times indispensable and which have made enormous strides in recent years, I would still remind the clinician that we must not expect the diagnosis to be handed to us ready-made from the laboratory.

THE USE OF STREPTOKINASE IN THE TREATMENT OF TUBERCULOUS MENINGITIS.[1]

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AND
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THOSE with experience in treatment of tuberculous meningitis welcome any suggestion which may improve the results of streptomycin treatment. With the appearance of an article by Cathie (1949*a*) interest was immediately aroused in the use of streptokinase, the activator of plasma fibrinolysin obtained from certain strains of hæmolytic streptococci.

The results of our treatment with streptokinase are inconclusive, largely because the period of observation of ten months from the time streptokinase was first used here is insufficient to assess the degree of permanent improvement in those patients who have so far survived.

[1] Part of this paper was read at a meeting of the Section of Pædiatrics, Australasian Medical Congress (British Medical Association), Seventh Session, Brisbane, May-June, 1950.

Nine patients have been treated; five are alive at present, of whom three have a reasonable chance of surviving with some permanent disturbance of the central nervous system. Results in treatment before the use of streptokinase are: 27 patients, five well for periods ranging from five months to two and a half years after cessation of treatment.

TABLE I.

Results of Streptokinase Treatment Combined with Streptomycin in Nine Cases; Five Patients Survived, Three of Whom Improved.

Name.	Age.	Day of Illness when Given Streptokinase.	Duration of Streptokinase Therapy.	Result.
Carmel L.	12 years.	For relapse after five months.	33	Death.
Joan V. ..	18 years.	7	15	Survival. Lower motor neuron paralysis of legs; 140 days' treatment.
Helen M.	7 months.	12	42	Death.
Anthony S.	15 months.	27	30	Survival; under treatment 50 days.
Janet H. ..	17 months.	15	40	Death.
John M. ..	13 years.	21	53	Condition deteriorating.
Charles L...	6 years.	20	63	Relapse; now under treatment again.
Irene S. ..	2 years.	20	24	Death.
James M. ..	2 years.	9	56	Condition improved; 102 days' treatment.

Preparation of Streptokinase.

Streptokinase, in a form which could be used clinically, was prepared at the Commonwealth Serum Laboratories. The organism used, H64, is a hæmolytic streptococcus of human origin, which produces streptokinase readily. Being a group C streptococcus, it is also free of any erythrogenic toxin factor. It was kindly forwarded to us by Dr. I. A. B. Cathie, from the Hospital for Sick Children, Great Ormond Street, London.

The methods used were largely a combination of the most practical ones available. Since 1939 at the Commonwealth Serum Laboratories it has been found that streptokinase is produced most abundantly in standard nutrient broth—a veal infusion, proteose peptone compound. Addition of phenol red as an indicator and of glucose as required allowed massive growth of organisms at 37° C., constant neutralization with normal sodium hydroxide solution being maintained. When growth was judged to have gone on sufficiently (usually about eight hours) the culture was rapidly chilled and left overnight at 2° C. It was centrifuged in the Sharples number 1 machine and only the clear filtrate was retained. This invariably was strongly fibrinolytic, possessing a titre of 1/256 to 1/512 when tested by Cathie's method (1949*b*). We have consistently found that this way of producing crude streptokinase broth is greatly superior to any of the existing published methods.

Purification of the streptokinase was first carried out by the procedure of Christiansen (1949), which involves fractional alcohol precipitation to remove impurities, especially desoxyribonuclease, which can be purified separately. This yielded a crude material which proved to have some irritant qualities when used clinically. However, further purification by application of the principle elaborated by Cohn for serum fractionation has allowed a product to be made which is substantially free of toxicity. The method here has merely been that of repeated low temperature alcohol precipitations at the correct pH and solvent concentrations, all other material being discarded.

The final streptokinase is dialysed with sterile precautions, since it cannot be Seitz filtered, and excess buffer

and "Merthiolate" is removed. After passing sterility and toxicity tests in mice, it is ready for use. It is in the form of an almost water-white solution, which is dispensed and freeze-dried in suitable amounts. Following Cathie, we have taken one intrathecal dose to be 100 times the amount of streptokinase needed to lyse the standard clot (one millilitre of a 1/20 dilution of fresh human plasma, clotted in saline); that is, one dose would lyse the clot from five millilitres of plasma, suitably prepared.

Clinical Nature of Streptokinase.

The present streptokinase may be introduced to the intrathecal space in twice the above dose without the production of a noticeable cell reaction in most cases. It also frequently prevents the formation of fibrin net seen in the cerebro-spinal fluid in some cases of tuberculous meningitis, notwithstanding the fact that no perceptible streptokinase remains in the cerebro-spinal fluid twenty-four hours after the dose—that is, in the sample withdrawn before the next dose is given.

Prepared by the above method, streptokinase mixes freely with the cerebro-spinal fluid and also with any of the three salts of streptomycin (sulphate, hydrochloride and calcium chloride) without forming any precipitate or gel. This latter effect has been mentioned by Cathie as having occurred; but we believe that our product is considerably more purified than those to which he refers, and have certainly not seen either opalescence or precipitation on mixing with any streptomycin or any mixture of the above salts of streptomycin.

The streptokinase solution on reconstitution from the dried state is relatively stable. Since excess buffer and antiseptic have been dialysed from it, and several doses are kept in the one vial, it is necessary to adopt completely aseptic precautions during reconstitution and the taking up of doses. Also it is essential to store the vial in a refrigerator between doses, if only to guard against possible growth of organisms introduced in this way.

Method of Treatment.

The diagnosis of tuberculous meningitis having been made, the patient is given 50 milligrammes of streptomycin intrathecally daily and 100 milligrammes three-hourly by intramuscular injection. Five millilitres of streptokinase solution are given intrathecally daily with streptomycin. This treatment is continued for two weeks, when streptokinase and streptomycin are given intrathecally on five days a week. Streptomycin is given by the intramuscular route six-hourly for a prolonged period, and after several weeks twice daily. The intramuscular dose of streptomycin is 0·02 milligramme per kilogram of body weight. Streptokinase is given at least twice weekly for a further two weeks, so that approximately a six-weeks period of streptokinase therapy is given.

Further treatment did not usually include streptokinase, and streptomycin administration was continued both intrathecally and intramuscularly for varying periods in this series up to 140 days.

With the first batch of streptokinase a rise in temperature was associated with the injection, and also an increase in cellular reaction in the cerebro-spinal fluid. The dose was reduced to 2·5 millilitres and no further reactions have occurred. A second batch of streptokinase prepared at the Commonwealth Serum Laboratories was considered most satisfactory from the standpoint of purity and absence of reactions when injected by either the lumbar or the ventricular route in a dose of 2·5 to 5·0 millilitres.

One child (Carmel L.) was first given streptokinase for a relapse occurring five months after the commencement of treatment of tuberculous meningitis and it was continued for thirty-three days. Further intramuscular streptomycin therapy was given, and two months later a second course of streptokinase was given for twenty-eight days, a dosage of five millilitres being used.

Discussion.

Examination of the brain of patients who have died of tuberculous meningitis shows a thick fibrinous basal exudate particularly in the interpeduncular region involving the optic chiasma. There may be accumulation in the longitudinal and Sylvian fissures involving the blood-vessels, and thrombosis of the arteries has been observed. It is reported that histological section of the gelatinous material shows an exudate consisting mainly of fibrin in which tubercle bacilli can be seen. Culture of the tubercle bacilli obtained *post mortem* has shown in most cases that the organism is sensitive to streptomycin even when the patient has received up to six months' treatment by the intramuscular and intrathecal routes.

It is a great deal to expect of this type of drug that, acting in the confined space of the spinal and cranial theca, and subject to the restrictions of flow of the cerebro-spinal fluid due to fibrinous exudate, it could gain sufficient access to the exudate to cause dissolution and allow streptomycin effectively to control the multiplication of the tubercle bacilli. That the fibrinolysin of the streptococcus named streptokinase by Tillett (Tillett and Garner, 1933) can cause such a dissolution of fibrinous exudate has readily been shown in the laboratory, and clinically in hæmothorax and empyema. Recently a similar process with an allied enzyme from the streptococcus named streptodornase by Tillett (Tillett *et alii*, 1950) has been effectively used for *débridement* of limb wounds.

In tuberculous meningitis it is reasonable to attempt to prevent thick exudate formation in the infratentorial areas anterior to the pons and around the medulla and spinal cord. In many instances it is the mechanical blockage rather than any toxic process that causes death. Cathie was encouraged by his results with streptokinase, and considered that by the use of streptokinase the duration of intrathecal therapy with streptomycin could be reduced.

The number of cases reported here is too few to support or deny the real value of streptokinase; but it is not dramatic in its effect, especially in the treatment of infants aged under two years. The product prepared at the Commonwealth Serum Laboratories is not toxic and can safely be given intrathecally for as long as eight weeks.

Early diagnosis and immediate commencement of intramuscular and intrathecal treatment with streptomycin alone, or in combination with streptokinase given intrathecally, before there is any great degree of blockage by fibrinous exudate either in the spinal theca or in the base of the brain, hold the best chance of success.

Because the results of treatment of tuberculous meningitis are far from satisfactory and because the combined intrathecal and intramuscular use of streptomycin and the exhibition of paramino salicylic acid are inadequate in many cases and the neurosurgeon is unable to overcome the mechanical difficulties due to the exudative accumulations, our impression is that streptokinase is worthy of further trial.

Summary.

Streptokinase is the fibrinolytic enzyme obtained from cultures of certain strains of hæmolytic streptococci. It can cause the liquefaction of fibrinous exudate *in vitro* and in the pleural cavity.

After the report by Cathie of its use in the treatment of tuberculous meningitis, streptokinase was prepared at the Commonwealth Serum Laboratories.

The results of treatment with streptokinase given intrathecally combined with streptomycin given intrathecally and intramuscularly are inconclusive. Of nine patients so treated, four have died and three have a chance of surviving with central nervous system disturbance. There is no toxic effect associated with the present batch of streptokinase when injected intrathecally.

The liquefying enzymes of the streptococcus have been shown to be of value in the treatment of exudative accumulation in hæmothorax, in empyema and on the surface of wounds of the limb. There is a distinct place for such an action in the treatment of tuberculous meningitis, indicating further trial with streptokinase. This should be combined with streptomycin given by intrathecal and intramuscular injection and paraamino salicylic acid given by mouth.

Acknowledgement.

We wish to thank the other members of the honorary medical staff of the Children's Hospital, Melbourne, for access to certain patients, and also Dr. H. McLorinan, the medical superintendent of the Queen's Memorial Infectious Diseases Hospital, Fairfield. The cooperation of the resident medical staff was appreciated, and we acknowledge their skill in the many thecal manipulations. Much valuable help came from the hospital pathologists, Dr. John Perry and Dr. Alan Williams, and their staff. The technical assistance in the production of streptokinase involved much painstaking work on the part of Mr. J. Thayer, of the Commonwealth Serum Laboratories.

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Reviews.

STATISTICS IN MEDICINE.

DR. RUTH RICE PUFFER, Director of Statistical Service of the Tennessee Department of Public Health, has epitomized her experience of the routine application of statistics to public health problems in a book, "Practical Statistics".[1] This covers chiefly the methods to be adopted in carrying out what appear to be, in America at any rate, routine investigations into such topics as the efficacy of diphtheria immunization, the infection rates in the relatives of tuberculous patients and so on. The beginner in this field will find much of value in the chapters on the planning of the investigation, the use of punch-card technique and a short non-mathematical chapter on elementary statistical techniques. The latter part of the book is directed towards several specific problems as examples of the methods used: prevalence data, the development of disease in observed populations, illness surveys, control of disease and follow-up campaigns, industrial health statistics. It can be recommended for workers in public health and hospital statistics.

HEALTH SERVICES IN NEW ZEALAND.

IN "Money, Medicine and the Masses", Dr. Albert D. G. Blanc has produced a masterly exposition of the medical and social aspects of personal and community life in New Zealand, particularly as altered by the *Social Security Act* of 1941.[2] The general theme running through this small book is that there should be no financial barrier between the patient and his attainment of complete medical care, a theme with which most people will agree. But whether the reader, lay or medical, agrees or not with the author's arguments, a thoughtful reading will be amply repaid.

In the first part of his book, Dr. Blanc discusses the patent medicine trade, certain popular fads and fallacies, and unqualified medical practice; he is very drastic in his criticisms. From this he progresses logically through the subject of the pharmacists and their relation to the health services, with a discussion on the manner in which they have improved their financial status, towards his second part, the State-controlled medical services. This part is opened by an account of the costs of pharmaceutical benefits in New Zealand, which skyrocketed from £279,698 in the first year, 1941-1942, to £1,558,350 in 1947-1948.

Dr. Blanc strongly supports the basic principle of State-controlled health services, and has high praise for the improvements which he states have taken place in New Zealand, but he just as strongly opposes the financing of these services on a fee-for-service system, which he is convinced has led to many of the abuses which he mentions. He develops his argument in favour of compulsory health insurance, with medical services paid on a salaried basis, and produces all the well-known arguments in favour of this system, many of which have been refuted by supporters of voluntary systems and other methods of payment.

This little book is well rounded off with its third part, which comprises chapters on general social medicine in New Zealand, with a good discussion on workers' compensation. Finally in a postscript the author summarizes and criticizes the Report of the Medical Services Committee of October, 1948.

A capably written book, this is one which should be carefully read by all thoughtful persons interested in the present world-wide debates on the organizing and financing of health services. Whether the reader agrees or disagrees with the basic thesis—and it is radically different from the general opinion in this country—his interest will be maintained from beginning to end, and the time spent will not be wasted.

DISEASES OF THE SKIN.

THE fourth edition of "The Common Diseases of the Skin" has been produced under the joint authorship of R. Cranston Low and G. A. Grant Peterkin, of the Edinburgh School of Dermatology.[1] The death of Dr. Low in February, 1949, removes the sole author of the first three editions. This is an excellent text-book for both general practitioner and medical students. The selection of the dermatoses, which are clearly described, includes all the most common. Again, as in the third edition, syphilis is not described, but mentioned only in differential diagnosis. Treatment is rightly restricted to a small but well-proven set of remedies. A greatly justified indictment of the local use of sulphonamides is stressed and, if it is heeded, much unnecessary suffering by patients will be avoided. Sections XI and XII are both devoted to "Scaly Eruptions". The inclusion in Section XII of such non-scaling dermatoses as leucoderma, scleroderma, cheiropompholyx, hyperidrosis, hypertrichosis and *hydroa vacciniforme* suggests the need for editing in future editions. For the treatment of *ulcus rodens* it is stated: "It has been found that very large doses of X-rays can be given with safety to rodent ulcers, e.g. 2,500 to 3,000*r* units." Australian dermatologists would regard these doses as of barely minimal carcino-lethal value and certainly not large. An appendix of "Useful Prescriptions" gives a number of well-selected formulæ in metric units. A short index completes the book; chance checking of this shows it to be accurate. Art paper is used and greatly enhances the reproduction of the nine colour plates and one hundred and thirty-nine black and white illustrations.

PHYSIOLOGY OF THE EYE.

"PHYSIOLOGY OF THE EYE" is being presented by Arthur Linksz in three volumes—"Optics", "Physiology of Vision" and "Biochemistry of the Eye".[2] The author describes his books as "An Introduction to Duke-Elder's Textbook, Volume I". They are not to be regarded as reference books, but as a means of informally introducing the scientific basis of ophthalmology. Each chapter is written in the style of a lecture. Even discussions with imaginery students are included to assist explanations.

Only Volume I—"Optics"—has appeared so far. It is of convenient size, particularly for students. The first section of 73 pages is devoted to physics of light. It forms an easy introduction to 100 pages of geometric optics. Mathematical formulæ have been reduced to a minimum and care

[1] "Practical Statistics in Health and Medical Work", by Ruth Rice Puffer, Dr.P.H., with a foreword by Hugo Muench, M.D.; 1950. New York, Toronto and London: McGraw-Hill Book Company, Incorporated. 8" × 5", pp. 252, with illustrations. Price: $3.75.

[2] "Money, Medicine and the Masses", by Albert D. G. Blanc, B.Sc., M.D., Ch.B., A.N.Z.I.C.; 1949. Wellington: A. H. and A. W. Reed. 7" × 4¾", pp. 212. Price: 10s. 6d.

[1] "The Common Diseases of the Skin: A Handbook for Students and Medical Practitioners", by R. Cranston Low, M.D., F.R.C.P.E., F.R.S.E., and G. A. Grant Peterkin, M.B.E., M.B., F.R.C.P. (Edinburgh); Fourth Edition; 1949. Edinburgh and London: Oliver and Boyd. 8¾" × 5¾", pp. 292, with 139 illustrations. Price: 21s.

[2] "Physiology of the Eye, Volume I, Optics", by Arthur Linksz, M.D., F.A.C.S., with a foreword by Walter B. Lancaster, M.D.; 1950. New York: Grune and Stratton, Incorporated. 10" × 7", pp. 252, with 137 illustrations. Price: $7.50.

has been taken to ensure their accuracy. The diagrams are outstanding in their originality, design and execution. It is a pity that many are on different pages from their references among the text. Page-turning to refer to diagrams disturbs reading; but this is a minor complaint. The eye as an image-forming mechanism is the subject matter for the 45 pages of the third section. The eye is therein analysed as a piece of optical apparatus. The statistical concept of errors of refraction is included.

The book is modern in thought and presentation, and the author deserves congratulation. It should be greatly appreciated by all ophthalmology students.

CHIROPODY.

THE second edition of "The Essentials of Chiropody" by Charles A. Pratt was published in 1949, and is a worthy successor of the edition published four years previously.[1] Essentially a book for the student of chiropody, it is well set out, clear, and, unlike many text-books, concise.

There has been very little alteration in the new edition, and the contents are set out in classified sections. The essential anatomy is well illustrated with appropriate diagrams; this is followed by an outline on the structure and function of the arches of the foot. The subject of footwear and the principles of treatment are dealt with before the pathological conditions which belong to the field of chiropody are described. The author is very careful to indicate the limitations of the chiropodist, and lays stress on conditions which should be referred for medical advice. It is noted that mention of the projecting tubercle at the base of a phalanx has been omitted again, when the soft corn is being discussed. The plantar wart is considered not to be within the field of chiropody, and the author advises "these cases should be referred to the doctor or electro-therapeutist". A full definition of the latter would have been a wise precaution.

Once more the book can be confidently recommended to students of chiropody as a sound and practical treatise on their subject. It is still produced in conformity with the authorized economy standards prevailing in England, but the paper, printing and binding are good. The price, however, is still relatively high and will cause some people to reflect before purchasing it.

CRIMINAL PSYCHIATRY.

FROM the tawdriest "whodunit" to the most advanced text-book of criminology, the subject of murder will always find a host of interested readers; and Frederic Wertham in "The Show of Violence" has provided a murderous meal for the jaded appetites of the curious, as well as a thoughtful book for those concerned with the problem.[2] The book might well have been subtitled "A Study of Murder", for each of the six case histories deals with murder and the psychiatric question as to whether the culprit was sane or insane at the time. The presentation of this material is not unattractive and is to some extent original. Names are fictitious, but the legal and clinical details are factual; and the writer displays a literary flair not only in the dressing-up of each story, but also by, here and there, interposing lines from the great Greek tragedy "Medea", tags from Shakespeare, Pope and others, and by opening his discussion with an italicized prologue embodying the Biblical account of the first murderer, and closing it with an epilogue (also italicized) in which he gives an affirmative answer to Cain's question.

This book is not intended exclusively for the psychiatrist. It is couched in ordinary speech; and while it has proved impossible not to use an occasional psychiatric expression, the general trend is well within the range of the educated layman. Before the cases are displayed the writer, an American psychiatrist of considerable experience, speaks "from the Courtroom". This chapter is necessarily didactic. It gives a clear history of the development of psychiatry in its association with jurisprudence. Its thesis is plain and plainly stated. If sufficiently provocative in style and content to make one think, it also carries a sense of conviction which appears difficult to gainsay. Some, no doubt, will find the writer at times egotistical in his opinions and unnecessarily cock-sure in his diagnoses in the later sections of the book. But it is obvious that he does not suffer fools gladly. He attacks institutions and individuals in the course of his criminal histories. He shows that justice is not always obtained. Imbued with a reformer's spirit, he pleads for the greater understanding of these criminal problems, the abolition of all laissez-faire methods and the continual display of that intellectual honesty which should characterize professional men.

This book is important, if for no other reason than that there is a murder committed in the United States of America every forty-five minutes; and that 60% of the murderers go undiscovered and unpunished. That is to say, every two hours of the day an American murderer commits the "perfect crime". There is magic in murder, sordid or fiendish though it may be. The impulse to kill, as Wertham shows, occurs in many forms and disguises. In the fantasies and dreams and in the neurotic behaviour of us all lie death wishes which may, in the appropriate social setting, unconsciously pattern murder in later life. Everyone in a murder trial, from the judge to the shorthand writer, and from the prosecuting counsel to the onlooker in the gallery, is emotionally involved. Murder is an experiment in time and place, for the dynamics of the crime are bound up with the social *milieu*. It is never, as this book shows, a purely psychological problem.

ARTHUR HURST.

IN recent months some of our ablest leaders in the medical profession have published articles in the various medical journals giving us pause to think upon the extraordinary developments that have taken place during the first half of the present century by a rapid extension of clinical knowledge, technical skill and scientific discovery in almost every branch of the healing art. Now we are privileged to view in retrospect the life and work of one of the most progressive and original of the distinguished physicians that Britain has produced in the period under review. For this unusual contribution to recent medical history we are indebted to Professor John A. Ryle, who occupied the Chair of Social Medicine in the University of Oxford until his death in February of this year. It was his aim to consecrate a long personal and professional association by editing the unfinished manuscript left by his old friend, Sir Arthur Hurst, and then to publish this entrancing autobiography under the appropriate title "A Twentieth Century Physician".[1]

In a gracefully written foreword, Professor Ryle tells us that, after his retirement from the staff of Guy's Hospital in 1939, Arthur Hurst devoted much of his spare time from literary and consulting work to the writing of his personal reminiscences until his death five years later. It seems that Hurst possessed a wonderfully clear memory, not only for cases and references, but also for events and places. He kept no diaries, and the only assistance he had was that provided by letters, publications and official records relating to landmarks of his own career. Professor Ryle felt no hesitation in persevering with the publication of the story of Hurst's life and times, for he thought it would have a wide appeal as the record of a new epoch in clinical medicine, while at the same time illustrating the emergence of a new type of physician.

Although Sir Arthur Hurst set out to tell the story of his own life, he reveals himself as a confirmed extrovert and looks out consistently on the medical world around him. Quite irresistibly he paints vivid pictures of settings in different parts of the old and new worlds where he made contacts with famous clinicians who were then making their contributions of new ideas to the rapid progress of medical thought. It has been said that the travelled mind is the catholic mind educated from exclusiveness and egotism; perhaps there was some such purpose behind the decision of Dr. John Radcliffe at the beginning of the eighteenth century to provide travelling fellowships for enthusiastic young physicians like Arthur Hurst.

The narrative begins with Hurst's family background as the son of a prosperous mercant of Bradford, his early

[1] "The Essentials of Chiropody", by Charles A. Pratt; Second Edition; 1949. London: H. K. Lewis and Company, Limited. 7¼" × 4¼", pp. 172, with 34 illustrations, some coloured. Price: 10s. 6d.

[2] "The Show of Violence", by Frederic Wertham, M.B.; 1949. London: Victor Gollancz, Limited. 8½" × 5½", pp. 290. Price: 15s.

[1] "A Twentieth Century Physician: Being the Reminiscences of Sir Arthur Hurst, D.M., F.R.C.P.; with a foreword by Professor John A. Ryle, M.D., F.R.C.P.; 1949. London: Edward Arnold and Company. 8½" × 5½", pp. 214, with illustrations. Price: 15s.

student days at Magdalen College, Oxford, and later as a medical student at Guy's Hospital, London, where as house physician he gained his Radcliffe Fellowship and membership of the Royal College of Physicians. The main part of the book treats most entertainingly of his experiences at famous medical clinics the world over and concludes with his work as a London physician from the days of the first World War to the year of his death in 1944.

This is a book to be read by all keen physicians with profit and pleasure, and there are many useful illustrations to amplify the text.

EINSTEIN GLEANINGS.

THE distinguished mathematical physicist, Albert Einstein, has gathered together a number of what may be called gleanings in his latest book "Out of My Later Years".[1] Some of these are brief introductions or five-minute addresses or short personal tributes to illustrious investigators in the domain which he has illuminated so notably, and are of value in demonstrating Einstein's essentially simple and generous nature. Others deal with the problems presented by his fellow Hebrews, and here it may be stated that his explanation of world-wide anti-semitic activity is as inadequate and unconvincing as similar statements made by Hebrew publicists elsewhere. For the prevention of war and the permanent establishment of international peace Einstein strongly favours a supranational government with a monopoly of armed force. This solution we may expect to find in the proposals of mere tiros in political science, the only novelty in the treatment of the theme being that Einstein realizes how determined Russia is not to adopt any such solution. He therefore suggests that the balance of the world should go ahead with the scheme, hoping that Russia may eventually join in. Some of the articles are frankly socialistic and one can realize why in certain circles of his adopted country Einstein has lately become unpopular. He writes reprovingly of the "dominant economic minority", of the evils of "the economic anarchy of capitalised society", of the direction of Press, radio, school and university by private capitalists and the inculcation into the American student of the worship of acquisitive success. Some Americans will applaud these utterances as proofs of moral courage; others, no doubt, will see in them bad taste and even ingratitude toward the country which gave him a refuge from tyranny and an income on which he could live with moderate comfort. It is, however, in the chapters on relativity and the fall of classical mechanics that his words will be most carefully pondered and critically appreciated. In his sketch of the rise of modern physics there is a modesty, almost a self-effacement, which must arouse respect. He begins with the uncanny intuitive principles of Faraday, who resented "action at a distance" and brought in his concept of "field". Clerk Maxwell followed, and though nominally an adherent of the Newtonian school, gave a mathematical structure to field mechanics and introduced the velocity of light as a fundamental unit in the cosmos. Then came Hertz, Lorentz, Planck, Schwarzschild and others. In classical mechanics space and time are separate and independent entities; in the newer physics the two form a continuum not merely as an algebraic device but as sound theory in the most approved scientific manner. In classical mechanics the coordinates were fixed; in modern field concepts coordinates are capable of movement, including uniform acceleration. A new and simpler approach to the equivalence of matter and energy is offered. It must be remembered in this connexion that the reason why no increase in weight has been measured following an increase in energy supplied is that the square of the velocity of light, an enormous figure, is now in the denominator of the equation and so the change in mass passes unobserved. Einstein's reaction to the quantum theory is interesting; he praises it for the solution of many problems, but seems in doubt whether it really fits in with his relativity scheme which deals with field concepts in pure space, whereas the quantum hypothesis is essentially particulate. Needless to say, some acquaintance with higher mathematics is assumed in the reader for the full understanding of the exposition, but the general drift can be grasped without this. The contents of the book were doubtless written originally in German; if so, the translation is admirable except that *resp.* (page 93) is not an abbreviation used in English and St. Mill (page 78) is a curious contraction for John Stuart Mill.

[1] "Out of My Later Years", by Albert Einstein; 1950. New York: Philosophical Library. 8½" × 5½", pp. 282. Price: $6.00.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Modern Practice in Dermatology, 1950", edited by G. B. Mitchell-Heggs, O.B.E., M.D., F.R.C.P.; 1950. London and Australia: Butterworth and Company (Publishers), Limited. 6¾" × 9¾", pp. 866, with illustrations. Price: 82s.

A member of the "Medical Practice Series".

"Textbook of Endocrinology", edited by R. H. Williams, M.D.; 1950. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Pty., Limited. 9¼" × 6", pp. 814, with illustrations, some of them coloured. Price: 95s.

Intended "to provide a condensed and authoritative discussion of the management of clinical endocrinopathies" in the light of chemical and physiological investigations.

"Techniques in British Surgery", edited by R. Maingot, F.R.C.S.; 1950. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 9¾" × 6¼", pp. 760, with many illustrations. Price: £7 2s. 6d.

Issued as "a liberal cross-section of British surgery as practised today".

"A Textbook of Gynecology", by A. H. Curtis, M.D., and J. W. Huffman, M.D.; Sixth Edition; 1950. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 9¾" × 6¼", pp. 824, with 466 illustrations, 37 coloured. Price: 95s.

Intended as a text-book for students and a guide for clinicians.

"The Task of Rationalism", by A. Gowans Whyte; 1950. London: C. A. Watts and Comuany, Limited. 7¼" × 5", pp. 28. Price: 6d.

Issued by the Rationalist Press Association.

"The Four Pillars of Wisdom: A Rational Approach to a Healthy Education", by Sir Sheldon F. Dudley, K.C.B., F.R.S.; 1950. London: Watts and Company, Limited. 7" × 5", pp. 268. Price: 8s. 6d.

The four pillars are semantics, psychology, statistics and logic.

"Steroid Hormones and Tumours: Tumorigenic and Antitumorigenic Actions of Steroid Hormones and the Steroid Homeostasis Experimental Aspects", by A. Lipschutz, M.D.; 1950. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 9" × 5¾", pp. 328, with many illustrations. Price: 64s. 6d.

To serve as an introduction to "a fascinating chapter of modern research on tumours".

"Tuberculosis and Other Problems of Pediatrics: The Abraham Flexner Lectures Series Number Ten", by A. Wallgren, M.D.; 1950. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 8" × 5", pp. 132, with illustrations. Price: 24s. 3d.

Comprises five chapters dealing with different subjects in pædiatrics.

"Huang Ti Nei Ching Su Wên: The Yellow Emperor's Classic of Internal Medicine", by I. Veith, M.A., Ph.D.; Chapters 1-34 translated from the Chinese with an introductory study; 1949. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson. 10" × 6¾", pp. 280, with illustrations. Price: 5s.

The translation "represents the approach of a medical historian rather than that of a Chinese philologist".

"Freud: Dictionary of Psychoanalysis", edited by N. Fodor and F. Gaynor, with a preface by T. Reik; 1950. New York: Philosophical Library. 8½" × 5½", pp. 228. Price: $3.75.

The author hopes "to correct the abundant misunderstandings and misconceptions among the intelligent people interested in psychoanalysis".

The Medical Journal of Australia

SATURDAY, NOVEMBER 4, 1950.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

DRUGS, DOLLARS AND IMAGINATION.

ONCE again we publish the account of a meeting of the Federal Council of the British Medical Association in Australia, but this time the meeting was a special meeting called to consider matters arising in connexion with certain government legislation with which most medical practitioners are familiar. The occasion is a good demonstration of the way in which the usual routine of two meetings a year may be upset. A routine which is never upset becomes like the law of the Medes and Persians "which altereth not". Not only that, but it may become a dull routine, than which there is nothing more depressing. No one who has attended the discussions of the routine meetings of the Federal Council can possibly describe them as dull. So many different points of view are presented from time to time on the most complex and difficult subjects and such ingenuity is shown in the finding of a solution that interest cannot flag. Even subjects on which all Branch representatives are agreed may call for finesse and wisdom to find a method of implementation that is both happy and effective. Matters which recur on the business paper may be prosy by reason of their recurrence, but here the fault nearly always lies with some authority or governmental department which displays silence or inertia either by design or because of an inherent inability to do anything else. People who do not wish the *status quo* of any undertaking or field of activity to be altered may or may not be dull; they often are. In order to stick to their routine they have to shut down on imagination. "Imagination", they say, "is all very well, but if we allow it free play, especially in those around us, they may get ideas and we shall have to change our ways and customs." These considerations are of considerable importance at the present time, especially in regard to one aspect of the working of *The Pharmaceutical Benefits Act*.

Readers will remember that in discussions with the Chifley Government when it wished to introduce what was known as "free medicine", the Federal Council made it clear that the members of the Association were of the opinion that certain "costly and life-saving drugs" might with advantage be supplied free of charge to the sick public. There is no need to describe the long arguments and discussions that were spread over some years, nor to mention again the legal processes and political actions that followed one another. It is sufficient to know that the present Government has introduced a measure by which "costly and life-saving drugs" may be supplied free of charge to everyone in the community and that the measure has the approval of the members of all six Branches of the British Medical Association through its representative Federal Council. The call to the practising members of the medical profession is now to see that the prescription writing under the provisions of the Act is conscientiously and wisely carried out. We all know that when people can obtain drugs for no immediate cash payment (the community pays collectively in the long run) their desire to have them increases—the story of drugs in New Zealand under the present national medical service in that Dominion shows this, if evidence of the statement is needed. The drugs obtainable under the present *Pharmaceutical Benefits Act*, however, are a special group and practitioners of medicine can largely, if not completely, control their use. In regard to those drugs which are in short supply—aureomycin, "Chloromycetin" and streptomycin—control is essential. Dr. A. J. Metcalfe, the Director-General of Health, has in a recent letter to the Editor of this journal (see THE MEDICAL JOURNAL OF AUSTRALIA, October 21, 1950, page 634) stated that not only has the need of the sick public to be met at present, but a reserve has to be built up in case war comes upon us. It is the duty of practitioners to see that the three drugs named are used only when no other drug will produce the desired result. A saving, small perhaps, but real, could be effected if the "overs"—the tablets or capsules not consumed by the patient—could be returned to the source of supply. Again, there is something in what Dr. Leigh Cook said at the Federal Council meeting on the effect of publicity in the Press of the results following the use of certain drugs. He mentioned the use of "Chloromycetin" in pertussis and the ease with which a demand for a drug could be created. Of course, the reply is that it is for the prescribing doctor to say what drug shall be used, but it may not be easy to refuse a persistent demand for a certain medicament in distressful circumstances when glowing reports of success about it have been circulated. The point is that if the medical profession sees that wise use is made of available drugs, and if the amounts available are not sufficient (there is little likelihood that they will be), the profession will have for presentation to the Government what should be an unanswerable argument. If the Government undertakes to supply to the people drugs which are known to be effective in certain pathological conditions it is stultifying and stupid on the part of the Government to allow supplies to be inadequate. We are told that it is a matter of dollars. The obvious thing to do is to spend more dollars on drugs. The Federal Council has been given to understand that the allotment of dollars to be spent by Australia on drugs will not be increased. This reminds us of the Medes and Persians, already mentioned. We may well ask what has happened to imagination. Would it not be better to spend fewer dollars on such imports as American cinematograph films of the, shall we say, less noble types, and more

on drugs that will stop some of our people from going to an avoidable grave? It is a matter on the one hand of the saving of lives and on the other the provision of silly films to amuse the multitude—bread and circuses all over again. The individual members of the community are not all lacking in intelligence; it is the instinct of the herd and of their factors which come into play. Public imagination on some vital matters lies dormant. Possibly the imagination of the public cannot be awakened, but politicians can claim no excuse for failure to display that important attribute. But the politicians have to be backed by a wise and efficient medical profession.

The other matters discussed at the Federal Council meeting which should be mentioned are those connected with the provision of a national medical service. Doctors generally and everyone in the community need to be impressed with the fact that agreement has been reached between the Government and the practitioner members of the medical profession through the Federal Council. Only by agreement between the Government and the profession can a satisfactory national medical service be provided. The decisions reached at the meeting in regard to the treatment of dependants of old-age, invalid and tuberculosis pensioners were right and it lies with the medical profession to stand behind the present proposals and to do everything possible to make them effective. The members of the profession must use their imaginations about the present and also about what the future may hold. No more need be said.

Current Comment.

A MEMORIAL TO A BELOVED TEACHER.

THE former colleagues of the late G. W. de P. Nicholson have created for him a memorial than which nothing more fitting could be conceived. During his lifetime he published from time to time in *Guy's Hospital Reports* "Studies on Tumour Formation"—some of them were discussed in these columns. Twenty of these essays have been published in a well produced and attractive volume.

The thesis pervading the book, presented with scientific precision and interwoven philosophical reflections, is that tumour formation should be considered not as an "abnormal" phenomenon, but as the outcome of the operation of biological rule. The author, by strictly objective and impartial reasoning, brings what he describes as the "orderly procession" of tumour formation into line with the successive stages in ontogeny, and defines for the genesis and growth of tumours, phases of induction, determination, and development, in the sense in which these terms are standard currency in biological science and applicable to normal organogenesis. It is cogently represented that tumours do not differ essentially in their structure and their growth from other tissues of the body. Typical tumours approach malformations very closely; so close is the relationship, indeed, that difficulty may often be experienced in deciding which of the two terms is the more appropriate to a particular deviation of tissue growth.

In an analysis of tumour formation by a mind deeply imbued with biological science, pathology is shown to be but a corner of the field of biology, offering, however, opportunities for gleanings of major importance in the sum of biological knowledge.

From an author with Nicholson's background an original approach to problems relating to tumour growth was to be anticipated. His book deals with such diverse and interesting subjects as the general structure of tumours, minor malformations, heterotopia, ectopic endometrial tumours, metaplasia, mixed tumours, and teratomata. He joins issue with orthodox teratology as based on the writings of Wilms, and dispassionately refutes such old-established tenets as the Cohnheim conception of "cell rests" and the closely linked Grawitz dogma regarding the nature of hypernephromata.

The literary style of the book, intimate and friendly, rich in philosophy, classical reference, and recurring touches of whimsical humour, was possibly determined in some measure by the fact that the author was writing for the magazine of his own hospital, and it is noteworthy that so well sustained is the theme that neoplasia is the expression of a physiological reaction on the part of the tissues to an "unphysiological" stimulus, that the twenty essays combine in a coherent text-book in which no hint is discernible that it was not originally designed as such. The work gains in individuality by the illustrations, all of which, in number 184, are the author's own beautifully executed drawings, which appear to have lost little or nothing in reproduction.

G. W. Nicholson's "Studies in Tumour Formation" is the product of an intellect of the first order, a penetrating though kindly exercised critical faculty, and the gift of lucid expression. The book could scarcely be digested by the average undergraduate, even were it not precluded by the capacity loading of the medical curriculum, but it should have a strong appeal to all whose interests incline them to post-graduate reading in pathology, and be accorded an honoured place in the libraries of all university and hospital departments concerned with the teaching of pathology.

DARWIN'S ORIGIN OF SPECIES: REPRINT OF FIRST EDITION.

A REPRINT of the first edition of Charles Darwin's great book "On the Origin of Species" antedates by some nine years the centenary of this truly epoch-making work. Yet the publication today is timely and a plea might have been put forward for the advisability of a still earlier issue. As is pointed out by Dr. C. D. Darlington, the well-known authority on genetics, in his able introduction, the first edition of November 24, 1859, represents the true Darwinian attitude; in subsequent editions Darwin bowed to the storm of criticism and admitted factors and qualifications we now know to have been unnecessary; for example, the inheritance of acquired characters, a doctrine forcibly advanced by Lamarck, is ignored or even rejected in the first but is introduced as possible in later editions. Today, with the exception of a few notoriety-hunters and a Russian school where political considerations dominate scientific, this theory of inheritance is set aside as false by modern biologists. Again, Darwin took to heart very much the criticism of Professor Fleming Jenkin, professor of engineering at Edinburgh, to the effect that any new variation would be swamped in later generations following crossing with the old and established type. As we now know, Mendel, who was really Darwin's contemporary, demonstrated that genetic factors remain unblended and untouched and free for natural selection to work on for generation after generation and thus the most effective criticism of Darwin's theory has been silenced. Further, Darwin, in order not to injure his case, left out certain speculations which aroused the ridicule of critics, even friendly critics; he need not have done so for the critics to whose judgement he was so deferential are now unregarded and unknown.

It is the sad fate of even the greatest scientific treatises to miss that permanent appeal retained by works of art

[1] "Studies on Tumour Formation", by the late G. W. de P. Nicholson, M.A., M.B., B.Ch.; 1950. London and Australia: Butterworth and Company (Publishers), Limited. 9¼" × 7", pp. 648, with 184 illustrations. Price: 82s.

[1] "On the Origin of Species by Means of Natural Selection, or the Preservation of Favoured Races in the Struggle for Life", by Charles Darwin, with a foreword by Dr. C. D. Darlington, F.R.S.; 1950. London: Watts and Company. 7½" × 5¼", pp. 450. Price: 15s.

—using the term in its widest significance. The noble "Principia" of Newton is scanned by only a very few historians of science and the contributions of Laplace, Young, Helmholtz and Kelvin are usually "taken as read". Once a new and important doctrine has been established in science few bother about its original introduction and proofs; further research is built upon it and so extreme modernity characterizes scientific literature. There are several features in Darwin's "natural selection" which seem "dated" when read today. His attacks, always calm and dignified, on the doctrine of special creation of all types of plant and animal, we pass over as no longer necessary as this doctrine is completely dead and discarded; but we are apt to forget that it was the one and only orthodox hypothesis of his day. The observations and opinions of men whose names are now forgotten may be found in many pages. There are evidences of hurry and we know that Darwin, much upset by Alfred Russell Wallace's anticipation of his views, rapidly assembled his best arguments and data and put aside the laborious collection of facts he had accumulated during a number of years. It was fortunate that he did so, for the book made a direct appeal to all sorts of thinking persons and not merely to expert biologists. No wonder the first edition was sold out on the day of its publication! The imperfection of the geological record he insisted on; that imperfection is much less significant today.

There are many excellences in this first edition not noticed by Dr. Darlington; chief amongst these is Darwin's admirable candour in presenting the difficulties of his hypothesis; in fact, many antagonists of evolution went to the volume itself for ammunition in the mighty battle which ensued and the misrepresentations and other unfair treatment of Darwin's arguments drove many a thinking young man into a militant rationalism. All through the book the temper of the author is superbly calm and free from cheap rhetoric; one may doubt if ever a work upsetting orthodox tradition has been so free from polemical taint. Another good quality, often praised deservedly, is the patience of the author collecting his facts from botany, zoology, geology, natural history, geography, and last but not least the lore of the breeder. The editing has been well done. A few slips have, however, crept in, but they are trivial blots in an otherwise noble reissue.

THE PARENTERAL ADMINISTRATION OF IRON.

THE best methods of administration of iron have been under intermittent discussion for some years. Admittedly the therapeutic use of iron can be properly discussed only in connexion with the pathology of the conditions in which it is observed, and the possible factors concerned in absorption of iron given by mouth must also be considered. Some years ago much more massive doses came into vogue than had been customarily used, although it was known that, while the amount of iron absorbed depended upon the amount administered, there was a limit in the practicable dose imposed by the capacity of the intestinal mucosa to accomplish absorption. Thus, multiplying an average dose by ten would barely double the amount absorbed. In addition, the digestive systems of many people rebel against salts of iron, and the chemical processes of the body were such that the gastro-intestinal tract was, so to speak, unimpressed by the pharmacological elegance of even expensive preparations, which received the same molecular adjustment in the stomach as the more humble salts. The war years will be recalled, during which certain favourite preparations of iron could not be obtained, though it was doubtful if the patients were any the worse. At intervals attempts have been made to give iron by parenteral injection, but usually the preparations employed gave toxic reactions when introduced intravenously, and enthusiasm has not been altogether maintained. Nils S. E. Andersson, of Stockholm, has published a monograph on his experimental and clinical investigations into the effect of parenterally administered iron.[1] In this he first traverses the history of the more recent work, beginning with the finding of Starkenstein that all complex iron compounds were absorbed after ionization with hydrochloric acid and reduction to bivalent iron. He mentions also the work of Hahn, Whipple and others with radioactive iron, which showed that absorbed iron was very quickly used in the synthesis of hæmoglobin, and that it was the depletion of depots of iron and some factor in the intestinal mucosa which regulated absorption, and not the degree of anæmia. Andersson points out also that the iron-protein complex "ferritin" has been shown to collect in the cells of the digestive tract, and that this substance appears to be the factor controlling mucosal absorption. Finally, the iron-binding capacity of the serum is important, possibly acting as a regulator of distribution, and excretion of iron from the body appears to be insignificant. After discussing the holding of iron in depots in the body, in the liver, the spleen and the bone marrow, Andersson goes on to relate what has been done to advance knowledge concerning the administration of iron by parenteral methods. As recently as 1946 investigators have reported that, in spite of the dramatic results obtainable from intravenous therapy, this method was inadvisable in the human subject on account of the severe toxic reactions encountered. The author has carried out experimental investigations on animals in which the iron content of the liver, spleen and bone marrow have been estimated, and has noted that the results are consistent as a rule within each animal species. Standard methods were used for determining the number of red blood cells, the hæmoglobin and the reticulocyte count. The particular point of this work is that it has been based on recently produced preparations of iron, linked to a soluble high molecular carbohydrate; the author has not experienced any serious immediate side effects from the use of these. He gives a full description of the methods used in animals and in man, and in addition to a control series of 70 healthy persons, has treated 83 patients suffering from iron deficiency due to hæmorrhages or to so-called "idiopathic" causes, and in a few cases, following resection of the stomach. Relapses occurred in some instances, the total number of treatments being 101. The average hæmoglobin concentration in the female patients was 11·5 grammes *per centum*, and in the males 13·5 grammes *per centum*: the corresponding figures for the controls were 13·8 and 15·6. The total amount of iron injected in each course of treatment was calculated to make good the hæmoglobin deficit and to allow for storage requirements. The therapeutic results were judged by the increase in hæmoglobin and the serum iron, the reticulocyte response and the improvement in the epithelial symptoms. These epithelial manifestations were of interest, for no fewer than 31 patients had some disturbance of the kind such as koilonychia, glossitis, dysphagia and cracks round the mouth. Full statistical information is given in appendices to this paper, and the author's contention regarding the value of intravenous therapy seems to be sustained. One point of importance is that of the possibility of toxic symptoms. Though Andersson's series has been investigated without significant toxic symptoms, some of the earlier batches of the drugs were not so blameless, but when new methods were used in the commercial processes these troubles were overcome.

It would seem wise to be sure that all due care is taken in the administration of iron by the intravenous route, but it would be strange if chemical and clinical research did not provide better methods for the treatment of resistant types of anæmia than we have had in the past. In conclusion, it may not be out of place to remark that discretion will always be advisable in the selection of patients to be treated with a single large dose of a potentially toxic substance, which should not be needed where the iron deficiency can be made good by a healthy and active reaction by the patient's own unaided bodily powers.

[1] *Acta medica Scandinavica, Supplementum* CCXLI, 1950.

Abstracts from Medical Literature.

PHYSIOLOGY.

Early Effects of Spinal Anæsthesia and Surgery on Blood Volume in Man.

L. S. MANN AND S. J. GUEST (*The American Journal of Physiology*, May, 1950) report results in a study of 25 patients who underwent arthrotomy, bunionectomy, osteotomy, lumbar sympathectomy, fusion of knee, inguinal herniorrhaphy, incision and drainage of foot, saphenous ligation, appendicectomy, skin graft and pilonidal cystectomy. "Seconal", morphine and scopolamine premedication with spinal "Pontocaine", glucose and ephedrine anæsthesia were employed in combination with standard surgical procedures. Determinations were made several days before surgery, ten to fifteen minutes after anæsthesia, and one hour after anæsthesia and surgery. The plasma volume showed no significant changes in the majority of instances ten minutes after anæsthesia, but there was a rise one hour after anæsthesia and surgery. The blood volume showed insignificant changes ten minutes after anæsthesia in most cases, but there was an increase in total circulating blood volume one hour after surgery and anæsthesia, which may have been possibly due to the effect of ephedrine. There has been no experimental work on the effect of ephedrine on blood volume. No fluids were given during the anæsthesia and surgery. The operative procedures were not extensive and blood loss was minimal. Those patients undergoing inguinal herniorrhaphy and lumbar sympathectomy in most instances did not show significant changes in blood volume. There was no significant change in plasma volume ten minutes after anæsthesia, but there was a rise one hour after anæsthesia and surgery in most of those patients receiving "Seconal", morphine and scopolamine premedication with spinal "Pontocaine" ephedrine anæsthesia. There was no significant change in blood volume ten minutes after anæsthesia. A rise in blood volume was noted one hour after anæsthesia and surgery in most patients receiving "Seconal", morphine and scopolamine premedication with spinal "Pontocaine" ephedrine anæsthesia.

An Attempt to Demonstrate Vascular By-Passes in the Kidney (the Trueta Phenomenon).

J. H. MOYER, H. CONN, K. MARKLEY AND C. F. SCHMIDT (*The American Journal of Physiology*, May, 1950) report that injections of indian ink into the blood flowing into the kidney during stimulation of the sciatic nerve yielded no evidence of the Trueta shunt phenomenon in either dogs or rabbits. The Trueta phenomenon could, however, be reproduced in rabbits (but not in dogs) after death, whether or not the animal's sciatic nerve had previously been stimulated. It could also be reproduced in living rabbits (but not in dogs) with small amounts of epinephrine. After electrical stimulation of the nerves surrounding the renal artery in rabbits there was a pronounced decrease in ink on the stimulated side as compared with the contralateral side, but no evidence of shunt was found. In both rabbits and dogs renal blood flow invariably decreased during sciatic nerve stimulation. Blood pressure rose in about three-fourths of the animals studied; in the remaining animals it either did not change or decreased. During sciatic nerve stimulation in both rabbits and dogs the renal arterio-venous oxygen difference consistently increased owing to a decrease in oxygen saturation of renal venous blood, as the renal blood flow decreased. Arterialization of blood in the renal vein never occurred as a result of sciatic nerve stimulation. After intravenous administration of epinephrine there resulted a consistent rise in blood pressure, decrease in renal blood flow and decrease in oxygen content of blood in the renal vein. The authors conclude that there is no evidence in these studies to support the hypothesis of an active patho-physiological renal vascular shunt following stimulation of the sciatic nerve or injection of epinephrine in rabbits and dogs.

Maternal Plasma as a Source of Iron for the Fœtal Guinea-Pig.

G. J. VOSBURGH AND L. B. FLEXNER (*The American Journal of Physiology*, May, 1950) state that the classical view that maternal red blood cells are the sole source of iron for the developing embryo and fœtus was derived from a considerable body of indirect evidence. Prior to 1925 efforts to demonstrate plasma iron had failed, and the view prevailed that the plasma was free of iron. It was consequently believed that the maternal plasma could not serve as a source of iron for the fœtus. On the other hand there was good reason to believe that maternal red blood cells were broken down in the placenta, releasing iron for the fœtus. The placenta was known to contain hæmolysins, hæmosiderin could be seen in it microscopically, iron could be demonstrated histochemically, and, in early stages of development, red cells could be seen apparently disintegrating within the parenchyma of the placenta or its sinuses. With the discovery that the plasma does contain minute amounts of iron, the view that the maternal plasma is an important source of iron for the fœtus became tenable, but even now it is not generally accepted. Evidence in favour of this view has been obtained with radioiron. When this tracer substance was given orally to women near term in pregnancy, measurable amounts were found in the fœtal blood forty minutes later. It was concluded that the appearance of radioiron in the fœtal circulation after this short interval suggests that it is derived from the maternal plasma. The authors have attempted to assess this theory quantitatively with radioiron during the last half of pregnancy in the guinea-pig, and have been able to demonstrate that sufficient iron is received from the maternal plasma to account for that incorporated during growth during the last half of the pregnancy.

Osmotic Analysis of Thirst in Man and Dog.

A. V. WOLF (*The American Journal of Physiology*, April, 1950) reports that various degrees of hypertonicity of body fluids and of thirst were produced in dogs and in man by means of intravenous salt water infusion. A thirst threshold was measured under these conditions in terms of a calculated relative decrease in the cellular water content, this value being called *r*. The value 100*r* is theoretically the percentage decrement in cellular water content at the thirst threshold. Calculations based on the osmometric equation are considered at present the most satisfactory means for investigating the cellular dehydration hypothesis of thirst. In the dog, an average for 100*r* of 2·15 ± 0·64% is believed to be in excess of the "true" thirst threshold. In man, 100*r* averaged 1·23 ± 0·48%, which is thought to represent an upper limit of the "true" thirst threshold. With reference to an osmometric thirst diagram, graphic and algebraic interpretations of problems in thirst are presented. These make use of equations of thirst and of isodipsic parameters. Hyperdipsic, hypodipsic and adipsic states are distinguished. The author states that while no primacy can be given to increased effective osmotic pressure of body fluids or to decreased cellular water content in initiating thirst, it is believed that either or both, when present to sufficient degree, can excite thirst. The cellular dehydration hypothesis is considered preferable to the "dry mouth" hypothesis, and it is suggested that particular osmoreceptors, probably in the central nervous system, and similar to or the same as those postulated by Verney, lie on the afferent side of a thirst reflex.

The Role of the Adrenal Glands in the Utilization of Oxygen.

M. A. GOLDZIEHER (*The Journal of Aviation Medicine*, April, 1950) states that air hunger is a conspicuous symptom in the adrenalectomized animal and in case of destruction of the adrenals in the newborn and, though less regularly, also in the adult. The physiological hypertrophy of the fœtal cortex is explained as a compensatory phenomenon due to the low oxygen saturation and tension of the fœtal blood. The physiological involution of the cortex after birth expresses the decreased need for cortical hormone upon onset of pulmonary respiration. The validity of this concept is confirmed by the absence of involution in the "blue baby". Tissues from adrenalectomized animals are lacking in the ability to use oxygen, but regain it when cortical extract is given. Oxygen consumption cannot be stimulated by the thyreoid hormone without the aid of the cortical hormone. Exposure to low atmospheric pressure induces cortical hypersecretion and eventually exhaustion of the cortex as an expression of the greatly increased demands for cortical hormone. Adaptation to long-continued exposure to oxygen deficiency is based on cortical hypertrophy and hypersecretion. Evidence of increased cortical secretion was obtained also in experiments on humans in which the influence of high altitude flying was reproduced. The adrenals react similarly with increased secretion if either the supply of oxygen is reduced or the demand for oxygen by the body is increased. The cortical hormone acts as a catalytic agent in the activation of enzyme systems in respect to both the metabolic effects and the regulation of the permeability of membranes. The secretion of the

adrenal medulla cooperates in the maintenance of tissue respiration, which thus appears as the function of the adrenal gland as a whole rather than of the cortex alone.

Effect of Humidity and Temperature on the Survival of Albino Mice Exposed to Low Atmospheric Pressure.

N. E. PHILLIPS, P. A. SAXON AND F. H. QUIMBY (*The American Journal of Physiology*, May, 1950) report the effects of variations in ambient temperatures (30° to −20° C.) and humidity (0% and 100%) on the ability of mice to withstand acute hypoxia. Mice in an atmosphere saturated with moisture were able to withstand significantly lower pressure than were those in a dry atmosphere at temperatures from 22° to −20° C. Also mice in moist air lost less moisture by evaporation than did those in dry air at temperatures below 22° C. Between 30° and 0° C. the ability of mice to withstand hypoxia increased with reduction in temperature. The beneficial effects of reduced temperature and increased humidity are explained as being due to a lowering of the energy metabolism requirements of the animals. Evidence is presented that at reduced pressure thermoregulation was lost and the resulting drop in body temperature correspondingly lowered the metabolic rate. Likewise increased humidity lowered the energy requirements by reducing the rate of vaporization of moisture from the body. Both factors thus reduced the requirements for oxygen and permitted survival to lower pressures.

BIOCHEMISTRY.

Uric Acid in Man.

W. GEREN *et alii* (*The Journal of Biological Chemistry*, March, 1950) have shown in man that orally administered uric acid is extensively degraded to urea, whereas intravenously administered uric acid is excreted essentially unchanged. The pool of available uric acid in man has been shown to be somewhat less than one gramme, and the half-life of this uric acid is less than one day (0·85 day). A method for the isolation of uric acid and a comparison of the uric acid content of normal human urine, as determined colorimetrically and by the isotope dilution technique, have been presented.

Methionine Formation.

J. A. MUNTZ (*The Journal of Biological Chemistry*, February, 1950) reports that rat liver homogenates incubated with choline and homocysteine form methionine, but dimethylaminoethanol, the expected product of the demethylation of choline, is not produced. Instead, dimethylglycine, the expected product of the demethylation of betaine, is formed. This suggests that in these systems choline does not lose a methyl group directly, but must first be converted to betaine before methyl transfer can occur.

The Mechanism of Secretion of Ions.

R. E. DAVIES AND A. G. OGSTON (*The Biochemical Journal*, March, 1950) present evidence of the differences of potential observed between pairs of calomel, silver chloride and glass electrodes when one of a pair is in the "nutrient" solution, the other in the "secretory" solution, of isolated, non-secreting gastric mucosa of the frog. The values of these potential differences and their variation with composition of the secretory solution have been interpreted in terms of the permeability of the mucosa to ions. An extended theory of the chemical and physico-chemical mechanism of gastric secretion has been developed, in the light of present knowledge of the chemistry and thermodynamics of cellular processes. This is shown to be consistent with the evidence available concerning gastric secretion. In the light of this theory, some other cases of ionic secretion are discussed.

Extrahepatic Synthesis of Cholesterol.

P. A. SRERE *et alii* (*The Journal of Biological Chemistry*, February, 1950) have shown that functionally hepatectomized rats can convert acetate to cholesterol. In addition to liver and adrenal, the following tissues of the adult rat are capable of converting acetate to cholesterol: kidney, testis, small intestine and skin. The brain and skin of the newborn rat also synthesized cholesterol. Surviving brain slices of adult rats completely failed to convert acetate to cholesterol. Hepatic and extrahepatic cholesterol synthesis is discussed.

Liver Lactic Dehydrogenase.

C. S. VESTLING AND A. A. KNOEPFELMACHER (*The Journal of Biological Chemistry*, March, 1950) report an assay for rat liver lactic dehydrogenase and a study of the properties of the system. A study has been made of the activity of rat liver lactic dehydrogenase at different levels of thyreoid function. Thyreoid administration resulted in a statistically significant decrease in enzyme activity. Thiouracil administration was accompanied by a small increase, and thyreoidectomy did not affect the rate of lactate oxidation in the liver homogenates. Experimental evidence is reviewed in support of the hypothesis that hepatic glycogenesis from lactic acid may be disturbed in hyperthyreoidism.

Hæm Synthesis.

I. M. LONDON *et alii* (*The Journal of Biological Chemistry*, April, 1950) have used isotopic nitrogen compounds to demonstrate that the immature non-nucleated rabbit erythrocyte is capable of synthesizing hæm *in vitro*. Using nucleated red cells from the duck, they have also shown the synthesis of hæm from glycine *in vitro*. This same system will incorporate the glycine into peptides. Serine is used for hæm synthesis only by being converted first to glycine.

Phospholipide Metabolism.

A. PIHL AND K. BLOCH (*The Journal of Biological Chemistry*, April, 1950) have studied the incorporation of isotopic carbon from labelled acetate into the fatty acids of neutral fat and of phospholipides in isolated liver and in the intact rat. In liver the rate of regeneration of neutral fat is faster than that of phospholipides. It is concluded that the phospholipides are not obligatory intermediates in the synthesis of triglycerides. In all other internal organs, including mesenteric fat, the isotope concentrations found in the phospholipides were much higher than in neutral fat.

Fatty Liver.

M. L. MONTGOMERY *et alii* (*The Journal of Biological Chemistry*, July, 1950) have identified trypsin as a possible intrinsic anti-fatty liver factor in the dog. The addition of as little as five milligrammes of trypsin to each lean meat meal fed to insulin-treated depancreatized dogs completely prevented the development of fatty livers.

Uric Acid.

M. GRIFFITHS (*The Journal of Biological Chemistry*, May, 1950) has shown that uric acid is diabetogenic in rabbits whose blood glutathione is lowered to about one-half the initial value by feeding a diet deficient in methionine and cystine. Under the same conditions xanthine and uracil are not diabetogenic. Uric acid is not diabetogenic in rabbits, whose blood glutathione is maintained within normal limits by feeding the diet deficient in methionine and cystine and modified by inclusion of extra protein. Cytologically, uric acid diabetes is similar to mild alloxan diabetes. The insulin content of rabbits and mice with uric acid diabetes and of rabbits fed a diet deficient in methionine and cystine is reduced to about one-third of that of normal rabbits. The insulin content of rabbits fed extra protein is substantially normal.

Bile Pigment.

I. M. LONDON *et alii* (*The Journal of Biological Chemistry*, May, 1950) have used labelled hæmatin to study the origin of bile pigment. They conclude that although the major portion of the bile pigment in man is derived from the hæmoglobin of mature circulating erythrocytes, a significant portion (at least 11%) is derived from one or more additional sources. In untreated pernicious anæmia a large part of the bile pigment is derived from one or more sources other than the hæmoglobin of mature circulating erythrocytes. The rates of formation and degraduation of uroporphyrin I and of coproporphyrin I in a subject with congenital porphyria were found to be rapid. A normal average erythrocyte life span of about one hundred and twenty days was observed in this subject with congenital porphyria. A large part, at least 31%, of the stercobilin in this subject was derived from sources other than the hæmoglobin of mature circulating erythrocytes.

Fatty Acid Transport.

I. BLOOM *et alii* (*The Journal of Biological Chemistry*, May, 1950) have studied the transport of labelled palmitic acid via thoracic duct and intestinal lymph of unanæsthetized rats. The rats received the palmitic acid either in the form of tripalmitin or as free fatty acid. In nineteen to twenty-four hours, 12 of the 14 rats studied absorbed from 81% to 95% of the administered fatty acid. From 70% to 92% of the absorbed palmitic acid was recovered as fatty acid from the thoracic duct lymph in nine of the ten rats studied. From 69% to 84% of the absorbed palmitic acid was recovered as fatty acid from intestinal lymph of four rats.

British Medical Association News.

MEETING OF THE FEDERAL COUNCIL.

A SPECIAL MEETING of the Federal Council of the British Medical Association in Australia was held at British Medical Association House, 135 Macquarie Street, Sydney, on September 23 and 24, 1950, SIR VICTOR HURLEY, the President, in the chair.

The General Secretary read the notice convening the meeting, and explained that it had been called at the request of the Queensland, South Australian and New South Wales Branch representatives.

Representatives.

The following representatives of the Branches were present:

New South Wales: Dr. A. J. Collins, D.S.O., M.C., Dr. W. F. Simmons, Dr. H. R. R. Grieve, Dr. A. J. Murray, O.B.E.

Queensland: Dr. A. E. Lee, Dr. H. W. Horn.

South Australia: Dr. L. R. Mallen, Dr. C. O. F. Rieger.

Tasmania: Dr. T. Giblin, Dr. J. L. Grove.

Victoria: Sir Victor Hurley, K.B.E., C.B., C.M.G., Dr. H. C. Colville, Dr. C. Byrne.

Western Australia: Dr. F. W. Carter, Dr. Leigh Cook.

Death of Dr. Reginald John Verco.

The President referred to the death of Dr. Reginald John Verco, which had occurred on June 5, 1950, and to the fact that he had been for a period of years a representative of the South Australian Branch on the Federal Council. The Federal Council resolved to place on record its deep sense of regret at the death of Dr. R. J. Verco, together with a minute of appreciation of the valuable services rendered by him to the British Medical Association and the medical profession in Australia.

Finance.

At the instance of Dr. W. F. Simmons, the Honorary Treasurer, the Federal Council discussed the allowances made to members attending meetings. It was pointed out that each member received the sum of 42s. for every night necessarily absent from home, and the sum of 42s. for each day necessarily absent from his practice. It was resolved that the amount should be increased to 63s. in each instance.

Dr. W. F. Simmons, the Honorary Treasurer, discussed the expenditure of the Federal Council for the year 1951, and moved that the *per capita* payment of the Branches should be at the rate of 21s. for each member on the membership list as at January 1, 1950. Dr. Simmons's suggestion was accepted.

Australasian Medical Congress (British Medical Association).

Seventh Session.

A communication was received from the Executive Committee of the Seventh Session of the Australasian Medical Congress (British Medical Association), held at Brisbane in May and June, 1950. The Executive Committee pointed out that a substantial profit had resulted from the congress dinner. This money was not part of the congress funds proper, and the Executive Committee thought that it might be used for the purpose of establishing an entertainment fund, not only for entertaining visitors to the sessions of congress, but also for entertaining important overseas visitors on other occasions. The Federal Council adopted the suggestion of the Executive Committee, and resolved to establish an entertainment fund, to be used for the purposes suggested.

Eighth Session.

A letter was received from the Victorian Branch, suggesting that the Eighth Session, which was to be held in Melbourne in 1952, should take place from August 22 to 30. The Victorian Branch also nominated Sir John Newman Morris to be president of the session. The Federal Council accepted the suggestion of the Victorian Branch in regard to the date of congress, and appointed Sir John Newman Morris as president.

Pharmaceutical Benefits Act, 1947-1949.

The Federal Council considered regulations issued under the *Pharmaceutical Benefits Act*, 1947-1949. Communications had been received from some of the Branches in regard to them. In view of the strong criticism made by the Western Australian and South Australian Branch Councils, the Federal Council resolved to ask the Minister that in future, before any regulations were issued, the Federal Council should be advised of the essential features of such regulations.

One of the provisions of the regulations was that any medical practitioner when prescribing benefits should place on the prescription form, including the duplicate, the words "pharmaceutical benefit". Unless this was done, the patient would not be entitled to the prescribed benefit. The Council of the Western Australian Branch viewed this provision with grave concern. It thought that the provision might have serious medico-political implications in the future. The question was raised whether the writing of the words "pharmaceutical benefit" on a doctor's prescription form made that form a government form. The Council resolved that a legal opinion should be obtained on this matter. The Council also resolved that if the reply was in the affirmative, an opinion should be sought as to how the purpose of the regulation could be effected without the doctor's form becoming a government form.

A discussion took place on the drugs included in the regulations under the Act, and it was explained that alterations would be made from time to time, additional drugs being included as were necessary. The Council determined that suggestions should be invited from its members in regard to anomalies that might exist under the regulations relating to the prescribing of pharmaceutical benefits under the Act, and that such suggestions should be supplied in writing to the responsible authority

It was reported that some medical practitioners prescribing the life-saving drugs which were the concern of the new Act were writing their prescriptions on the old government forms issued by the previous Government in connexion with the old Act. Dr. H. C. Colville said that this practice was fraught with the gravest danger, and was one of extreme unwisdom. The same view was expressed by Dr. Leigh Cook. The Federal Council resolved to recommend to members of the Association throughout Australia that they should use only their own forms for prescribing under the Act.

The General Secretary referred to the list of pharmaceutical benefits, and said that he had received a letter from the Director-General of Health, advising of the intention of the department to publish at an early date a consolidated list of pharmaceutical benefits including all amendments.

The General Secretary referred to the position of medical practitioners under the Act who lived in an area in which there was no approved pharmaceutical chemist, and who did their own dispensing. He pointed out that these practitioners would have to obtain the approval of the Director-General of Health if they desired payment from the Department of Health for pharmaceutical benefits supplied to patients. He said that a paragraph dealing with this matter had been sent to the Editor of THE MEDICAL JOURNAL OF AUSTRALIA for publication. The statement was published in the issue of September 9, 1950, at page 424.

Reference was made to the supplying of drugs to medical practitioners by wholesalers. Medical practitioners who wished to have on hand supplies of drugs for use in their practice were now compelled to go to a retail chemist, as the wholesaler had no power under the Act to supply the practitioners. The General Secretary said that he understood that the matter was being looked into.

Reference was made to the control of drugs which were in short supply, such as aureomycin, "Chloromycetin" and streptomycin. The General Secretary said that he and Dr. A. J. Collins, the Vice-President, had had a conference with the Director-General of Health on the subject. He had also had some correspondence with the Director-General. The department was concerned about the shortage, and the Director-General thought that perhaps the Federal Council could suggest something that might be done. The General Secretary said that there were several possible methods of control. These included the issuing of the drugs to hospitals only, and in this case medical practitioners requiring the drugs would have to obtain them from the hospitals in their area. Another method was by the appointment of a committee, which would issue the drugs to applicants on being convinced that the patient for whom they were intended would benefit by their administration. Dr. A. J. Collins said that there should be some form of committee

control. Dr. A. E. Lee said that the Queensland Branch was opposed to the appointment of a committee. The Queensland Branch thought that someone on the Federal level should determine what drugs were in short supply. A committee in control would have to know to what uses the drugs were to be put. It was difficult to know how to limit the use of these drugs. The Queensland Branch was not happy about the issuing of certificates. The Federal Government should publish to the profession and to the public what drugs were in short supply, and practitioners should be compelled to justify their use. Dr. Leigh Cook referred to the harm done by publicity in the Press on the good results of the use of certain drugs. As an example he quoted reports on the successful use of "Chloromycetin" in pertussis. The result was an immediate rush for supplies of "Chloromycetin". The creation of a demand for such a drug was very easy. Dr. W. F. Simmons said that the New South Wales Branch would be quite happy with the appointment of a committee. Dr. A. J. Collins remarked that care had been taken to obviate any suggestion of disciplinary control. After further discussion the Federal Council resolved that a Federal Government authority should state to the medical profession and to the public what drugs were in short supply. It also resolved that an expert committee on the Federal level should determine and inform the medical profession for which diseases the drugs in short supply might be justifiably used. It further advised that a committee should be appointed in each State to control the distribution of aureomycin, "Chloromycetin" and streptomycin, and other drugs declared to be in short supply. A motion to the effect that doctors who used the drugs unjustifiably should be called upon to appear before a disciplinary committee was lost. It was resolved on the motion of Dr. Leigh Cook, seconded by Dr. F. W. Carter, that, pending the appointment of these committees, members of the medical profession should be circularized and be urged to exercise discretion in the prescribing of drugs in short supply, and also in view of the necessity of the conservation of supplies in the event of the occurrence of war.

A discussion took place on the manufacture of drugs in Australia, and the Federal Council resolved to advise the Minister for Health that it was of the opinion that immediate steps should be taken to arrange for the manufacture in Australia of those life-saving drugs that were in short supply, and which at the present time were obtained from overseas.

The Federal Council resolved to recommend to the expert Federal committee to be appointed that consideration should be given to the suggestion that, when practicable, in-vitro sensitivity tests should be conducted in each case before drugs declared to be in short supply were prescribed.

A discussion took place on the cheapness of drugs, and reference was made to the great variation in prices of one drug manufactured by different manufacturing houses. Dr. H. R. R. Grieve thought that the price should not be published, as publication might be regarded as a suggestion that the cheapest drug should be ordered. This in his opinion was an interference with the freedom of the practitioner to prescribe any drug which he thought necessary. Dr. H. C. Colville agreed with Dr. Grieve. Other members of the Federal Council thought that the publication of prices might have the opposite effect, and that practitioners would prescribe the dearest drug because they thought it was therefore the best. Dr. A. J. Collins said that he thought that the prices should be given, because the difference in price was not always justified. The Federal Council therefore resolved to ask the Federal Government to include the price of drugs in the list of pharmaceutical benefits for the information of members of the profession.

Discussion took place on the appointment of committees to deal with abuses under the Act. Dr. A. J. Collins said that no such committees should be appointed until the new Act had been introduced. Dr. A. J. Murray said that the committees of the kind under discussion should be called "reference committees". It was pointed out that the Minister had no power to appoint such committees under the Act. It was resolved to recommend to the Minister the setting up in each State of pharmaceutical benefits committees.

The General Secretary raised the question of the constitution of the Formulary Committee. Dr. F. W. Carter opposed the equal representation of medical practitioners and pharmacists on the formulary committee. He pointed out that, having regard to the benefits provided, there was no need for pharmacists to be on such a committee. Dr. A. J. Collins pointed out that the only advice needed at the present time by the Government was in regard to therapy. It was resolved, on the motion of Dr. Collins, that the Federal Council was of the opinion that, having regard to the government policy of limiting pharmaceutical benefits to the costly and life-saving drugs, there was no need for a formulary committee as specified in the *Pharmaceutical Benefits Act*.

Reference was made to the fact that some of the drugs supplied under the Act might be used for the treatment of persons suffering from drug addiction. The Federal Council resolved to recommend to the Minister for Health that the supply of dangerous drugs for the purpose of treatment of subjects of addiction should not be allowed under the *Pharmaceutical Benefits Act*.

National Health Service.

Medical Service to Pensioners.

At its previous meeting in May, 1950, the Federal Council had agreed to accept a concessional rate for a service to old-age, invalid and widow pensioners. Since that time the Minister had indicated that he wished to include in the service tuberculosis pensioners and dependants of all pensioners. The General Secretary said that he had referred this matter to the Branches and had received replies. All the Branches had approved of the extension of the service to tuberculosis pensioners and the dependants of pensioners, with the exception of the Victorian Branch, which did not agree that a concessional service should be given to pensioners' dependants and to those in receipt of allowances under the *Tuberculosis Allowances Act* and their dependants. The number of pensioners in the pensioner group had been estimated as at December 31, 1950. The number of old-age pensioners was 334,000; the number of invalid pensioners was 12,000; the number of tuberculosis pensioners was 4800; a total of 466,800. The number of dependants, wives and children of all these groups with the exception of the tuberculosis pensioners was 150,000. The number of dependants of tuberculosis pensioners was: wives, 1585; children, 1863; a total of 3448. The Western Australian Branch disapproved of the administration of a pensioner service by a government department. The Western Australian Branch also opposed the formation of any government department for a pensioner medical service, even as a temporary measure, until those regulations which directly affected doctors, and which had been issued without the approval of the Federal Council, or its full executive, and also those which had been issued concerning pharmaceutical benefits, were withdrawn. After considerable discussion the Federal Council agreed to the inclusion in the pensioner medical service of service pensioners, of tuberculosis pensioners, and of the dependants of all pensioners. The Federal Council agreed that the scope of the service should be that of the Common Form of Agreement between a medical officer and a friendly society lodge, and such other services of a minor or special character as were ordinarily rendered in the surgery or in the home. The Federal Council expressed the opinion that the fees paid to medical practitioners for attendance on pensioners should vary with the basic wage and should be reviewed every six months. The Federal Council was also of the opinion that if the means test for pensioners was liberalized or abolished, the whole question of concessional services would have to be reviewed.

The Federal Council discussed the method of payment of a pensioner medical service. It expressed the opinion that as it was at present impracticable for payment for medical services to pensioners to be paid through approved medical benefit organizations, as had been resolved at its meeting in May, 1950, payment should be made directly to medical practitioners through a government department. After discussion the Federal Council expressed the opinion that payment to medical practitioners for attendance on pensioners should be made on production of a voucher signed by the patient and by the medical practitioner, in which the patient assigned to the medical practitioner his right to the benefit given. The Federal Council resolved to ask the Minister for Health to delete from the payment voucher the time of attendance.

The Federal Council resolved that the method of ascertaining the names of those medical practitioners willing to cooperate in the provision of pensioner medical services should be by means of a notice issued by Branch offices of the British Medical Association, asking members to advise such offices of their willingness to cooperate. The lists would subsequently be forwarded to the Department of Health. The Federal Council disapproved of any rule or regulation which would require a medical practitioner willing to participate in the provision of a pensioner medical service to complete a government form agreeing to render general practitioner service subject to terms and conditions

laid down. It thought that pensioners should be handed a list of participating medical practitioners in the area in which they resided, on the understanding that the department could not be held responsible for the payment of mileage if a pensioner desired to be treated by a medical practitioner of his choice outside the area.

The Federal Council approved of the appointment of committees to deal with abuses which should have statutory powers of the type laid down by the Federal Council in relation to the *Pharmaceutical Benefits Act*. It decided to suggest to the Minister for Health that Branch Councils of the British Medical Association should be asked to nominate members of the committee in each State, the number of members of each committee not to exceed five.

The Federal Council held that administration of the pensioner medical service should be by the Department of Health, and not by the Department of Social Services. The Federal Council expressed the opinion that, if the Federal Government wished to extend the scope of pharmaceutical benefits to pensioners beyond the life-saving and disease-preventing drugs now available under the *Pharmaceutical Benefits Act*, such extension of benefits should include any drugs in the British Pharmacopœia, to be prescribed in the dosage and the form considered necessary by the medical practitioner. The Federal Council also resolved that if the Minister for Health wished to provide additional pharmaceutical benefits to pensioners, it would recommend to members of the medical profession that, if the Minister so desired, prescriptions should be written in duplicate and so marked as to identify them as pharmaceutical benefits for pensioners.

Form of Administration.

At its meeting in May, 1950, the Federal Council considered a memorandum by the Western Australian Branch on the administration of a national health service. The General Secretary reported that the Branches had not been in favour of the Western Australian scheme. The Federal Council had before it a series of recommendations from the New South Wales Branch. These were to the effect that for the purposes of administration there should be a Federal statutory committee of medical services, with State committees having delegated powers. The Federal statutory committee should have control of the medical services. It should be responsible to the Minister for Health, but should have complete autonomy in administering funds appropriated to it, so long as its decisions were consistent with the broad lines of policy laid down in the Act for a national health service. In addition it should have power to initiate advice to the Minister on all matters relating to medical services carried out by the Government. The New South Wales Branch suggested that the statutory committee should consist of five members, one a representative of the Treasury, one the Director of National Medical Services, and three other representatives of the profession in private practice. These three representatives should be appointed part time on the nomination of the Federal Council. The initial appointment should be for periods of three, four and five years for each of the three appointees, and thereafter for a period of three years. It was resolved on the motion of Dr. H. R. R. Grieve that the recommendations of the New South Wales Branch, together with a copy of the resolutions of the meeting of the Federal Council of December 11, 1948, should be referred to the Branches for their consideration. (For these resolutions see THE MEDICAL JOURNAL OF AUSTRALIA for April 15, 1949, page 531.) The Federal Council also resolved that legal advice should be sought regarding the drafting of the constitution of a corporate body of control of a national health service with a minimum of political control.

Publicity.

Reference was made to a statement by Mr. Eric Scott, Federal President of the Federated Pharmaceutical Service Guild of Australia, which had been published in the *Pharmacy News Bulletin*. The New South Wales Branch reported that the editor of the *Pharmacy News Bulletin* had failed to withdraw or to correct the statement. The New South Wales Branch had written to the Pharmaceutical Society of New South Wales, and had asked in what way it was related to the Federated Pharmaceutical Service Guild of Australia. The Pharmaceutical Society had replied that it was a completely different organization from the Federated Pharmaceutical Service Guild of Australia, and that there was no way in which the society could be represented on that body. The Pharmaceutical Society did not approve of the action of Mr. Eric Scott in publicly criticizing the policy of the British Medical Association. The action of the New South Wales Branch was endorsed. The Federal Council also resolved to inform the Branches that it was of the opinion that, in respect of liaison with the pharmaceutical profession, such liaison should be with the Pharmaceutical Society in each State, and not with the Federated Pharmaceutical Service Guild of Australia.

British Commonwealth Medical Conference.

At its previous meeting the Federal Council resolved that it would be represented at the third annual British Commonwealth Medical Conference, to be held at Johannesburg, South Africa, in July, 1951. The Federal Council resolved that Dr. J. L. Grove should be appointed its representative to attend the gathering.

Repatriation Department.

Fees Payable to Local Medical Officers.

The General Secretary reported that no reply had been received from the Repatriation Department in response to the Federal Council's repeated request for adjustment of fees payable to local medical officers of the department. The Federal Council resolved that the Minister for Repatriation should be informed that, unless a satisfactory reply was received by January 1, 1951, to the representations of the Federal Council in regard to fees payable to local medical officers, the Federal Council would reluctantly be compelled to advise members of the medical profession not to accept appointment as local medical officers.

The Treatment of Civilian Patients in Repatriation Hospitals.

Further reference was made to the treatment of civilian patients in repatriation hospitals. The General Secretary said that he had received letters from some of the Branches dealing with the matter. The South Australian Branch had replied that civilians were not treated in repatriation hospitals in that State. The Victorian Branch suggested that a legal opinion might be obtained regarding the power of the Repatriation Department under the *Repatriation Act* to admit to repatriation hospitals persons suffering from conditions other than war disabilities. The Queensland Branch thought that an effort should be made to obtain an agreement on the matter. Dr. H. W. Horn said that at the present time there was no agreement at all for any treatment undertaken at repatriation hospitals. There was a shortage of hospital beds in the community, and the repatriation hospitals had beds available. If an agreement was made, it might be possible for these beds to be used. Dr. A. J. Collins said that he had been asked to treat Balts at a repatriation hospital, and had refused to do so. He thought that a separate arrangement could be made in regard to the treatment of civilians. He said that among the people who were being treated were the widowed stepmothers of deceased unmarried soldiers. The Federal Council resolved to approach the chairman of the Repatriation Commission on behalf of the visiting staffs of repatriation hospitals, with a view first to the making of an agreement for the treatment of personnel under repatriation entitlement, and secondly, in order to discuss the treatment of civilian patients who were not so entitled. It was resolved that the President, Sir Victor Hurley, and Dr. H. C. Colville should interview the chairman of the Repatriation Commission.

Commonwealth of Australia Jubilee.

The General Secretary reported that he had received a letter from Professor R. C. Mills, Convenor of the Education and Science Committee, inquiring in regard to any contribution which the British Medical Association in Australia might make towards the celebration of the Commonwealth of Australia jubilee. The General Secretary said that he had written to the Branches on the matter, and added that he had received a letter from the Editor of THE MEDICAL JOURNAL OF AUSTRALIA, stating that a Commonwealth jubilee number of the journal would be issued on January 6, 1951.

Alien ("New Australian") Medical Practitioners.

The General Secretary reported that the President had received a letter from the Minister for Immigration, asking the Council's views on the need for and the practicability of obtaining some greater measure of recognition of the medical qualifications of foreign migrants, and on the manner in which such liberalization could best take place. After discussion the Federal Council resolved that a committee, to be known as the Migrant Doctors Committee, should be appointed to report on the proposal of the Minister for Immigration, and that the committee should deal specially

with the following four aspects: (i) the number of medical practitioners likely to be required for the population in the next ten years; (ii) the capacity of Australian universities to fill these needs; (iii) the number of British migrant medical practitioners that could be attracted to Australia; (iv) what gap, if any, there would remain for the absorption of foreign medical practitioners. It was resolved that the President, Sir Victor Hurley, the Vice-President, Dr. A. J. Collins, Dr. H. R. R. Grieve and Dr. A. E. Lee should be appointed members of the Migrant Doctors Committee, and that they should have power of cooption.

Administration and Organization of Commonwealth Health Services.

At its previous meeting the Federal Council had resolved to offer to the Commonwealth Government the services of leading members of the medical profession, if desired by the Ministers concerned, for the purpose of inquiring into the administration and development of the Commonwealth medical services including repatriation. This matter was further discussed, and information regarding medical services of the Repatriation Department was laid before the Federal Council. The Federal Council resolved that the Minister for Repatriation should be informed that the Federal Council was of the opinion that the medical service of the Repatriation Department had become so important and had expanded in so many directions that it should be a separate department. The Federal Council therefore recommended that there should be established a department of Repatriation Medical Services, and that this department should be under the control of a medical man as Director-General of Repatriation Medical Services, with direct access to the Minister for Repatriation and to the Commonwealth Public Service Board. The Federal Council resolved to send a copy of this recommendation to the chairman of the Repatriation Commission. It was resolved that the Minister for Repatriation should be interviewed on the matter, and that if the interview took place in Melbourne, the President, Sir Victor Hurley, and Dr. H. C. Colville should represent the Federal Council; if, on the other hand, the interview took place in Sydney, the Vice-President, Dr. A. J. Collins, and the General Secretary should conduct the interview.

The Examination of Recruits for Compulsory National Service.

The General Secretary said that at the beginning of the year 1951 the Commonwealth Government would be calling up from time to time batches of recruits for compulsory national service. These recruits would have to be medically examined. The Department of Labour and Industry, which would be responsible for the call-up of recruits, was anxious to secure the cooperation of the medical profession and desired the Council to name a fee which would be acceptable to medical practitioners undertaking this work. It was desired that the work should be undertaken in evening sessions of two and a half hours by practitioners in private practice. The matter had been mentioned a few days previously at the conference of delegates of the Local Medical Associations with the Council of the New South Wales Branch, and divergent opinions had been expressed. On the one hand it was thought that the fee should be five guineas for the first two hours and two guineas for every subsequent hour or part thereof. On the other hand one Council representative had suggested that the work should be done by medical practitioners as a national gesture in a voluntary capacity. In discussion the Federal Council resolved that only a small fee should be charged, and it was decided that this should be two guineas for the first hour and one guinea for every subsequent hour or part thereof.

Votes of Thanks.

A vote of thanks was passed to Sir Victor Hurley, the President, for having presided at the meeting. The Federal Council thanked the New South Wales Branch Council for its hospitality and for the use of its offices. It also thanked Dr. A. J. Collins and Dr. A. J. Murray for their hospitality. The Federal Council thanked Dr. J. G. Hunter and Miss Cameron for their services during the meeting.

Date and Place of the Next Meeting.

The date and place of the next meeting were left in the hands of the President.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on June 22, 1950, at the Royal North Shore Hospital of Sydney, Crow's Nest, New South Wales. The meeting took the form of a number of clinical demonstrations by members of the honorary medical and surgical staff of the hospital. Part of this report appeared in the issue of October 21, 1950.

Carcinoma of the Larynx.

DR. J. B. DOWE presented a man, aged sixty-two years, who, when first examined, had noticed huskiness of the voice intermittently for three years, and persistently for three months, but no pain, stridor or dyspnœa. On examination, the patient had an irregular ulcerated carcinoma of the anterior half of the right vocal cord, extending to the anterior commissure and just across the mid-line. The growth extended superiorly to the ventricular fold and into the subglottic space for a distance of five millimetres. Partial fixation of the cord was present. There were no palpable gliomata. Biopsy revealed squamous carcinoma. In November, 1948, total laryngectomy was performed through a mid-line incision, with subperichondrial dissection and preservation of the pretracheal muscles (the so-called "narrow field" technique). On the third post-operative day there was a leak of mucus at the site of the drainage tube, but that subsequently closed. On the seventh day a fistula developed into the posterior aspect of the trachea at its junction with the skin (a pharyngo-tracheal fistula). That necessitated frequent aspiration of mucus from the trachea. In December, 1948, suture of the pharyngeal aspect of the fistula just below the tongue was carried out. Mucus continued to drain for two weeks, and then the fistula appeared to be healed. The feeding tube was removed and the patient was discharged from hospital. He had been well since, but scar-tissue contraction around the tracheal stoma necessitated the presence of a tracheotomy tube for most of the time. He had recently decided to try to learn to produce a pharyngeal voice and was being instructed by a speech therapist.

Actinomycosis.

DR. L. S. LOWENTHAL presented a woman, aged forty-nine years, with actinomycosis. In July, 1949, the patient had suffered from acute appendicitis with rupture of the appendix and peritonitis. For that the peritoneal cavity had been drained and a portion of the appendix removed. In December, 1949, the patient had again presented herself with general peritonitis, and again the peritoneal cavity was drained. Gross œdema was found on the left side of the pelvis. On April 20, 1950, she was admitted to the Royal North Shore Hospital of Sydney, complaining that since December, 1949, she had had an abdominal sinus discharging pus. Abdominal pain, present in the left hypochondrium, was relieved by the passing of flatus, but this flatus was troublesome to her, and its passage was frequent. The action of the bowel was regular, neither constipation nor diarrhœa being present. The patient was deaf. On examination, the patient was found to have a mid-line abdominal scar with two discharging sinuses on either side and a third about three inches to the right of the mid-line. A large, firm mass was palpable in the left hypochondrium and to the left of the umbilicus. It was tender, had a smooth surface notched medially, and was quite mobile. The liver was not palpable. Rectal examination revealed no abnormality. Pus from the sinuses was yellow and watery and contained blood and yellow granules. X-ray examination after a barium enema revealed no evidence of sinus communication with the bowel, but a small diverticulum was present. Lipiodol was seen to flow through an abdominal sinus into a cavity lying in the region of the left sacro-iliac joint, but the cavity had no connexion with the large bowel, and indeed was quite superficial, being confined to the abdominal wall. The urine was sterile. The results of tests for syphilis and hydatid disease were negative. The hæmoglobin value was 11·9 grammes *per centum*. The total number of leucocytes was 14,200 per cubic millimetre, 74% being neutrophile cells, 15% lymphocytes, 5% monocytes, 2% eosinophile cells and 4% band forms. Pus from a sinus was found to contain Gram-positive filaments, some with clubbed ends. "Variation" from coccoid to bacillary forms was present. No branching was observed, and on attempted culture no *actinomyces* were grown. The sinuses were explored in the operating theatre, and were found not to communicate with internal organs. A needle was passed into the mass in the left side, and blood was withdrawn. On May 24, 1950, treatment was commenced with penicillin, five mega units per twenty-four

hours being given. By June 7, 1950, the mass in the left loin had subsided to a great extent, and was less tender than on the patient's admission to hospital. An excretion pyelogram revealed poor kidney function, but normal pyelographic appearances.

Ulcerative Colitis.

Dr. Lowenthal's next patient, a boy, aged twelve years, had been well until the age of five years, when he began to pass blood intermittently *per rectum*; this lasted until he was aged seven years. Then he was admitted to the Royal Alexandra Hospital for Children with anæmia and diarrhœa. One year later he had an attack of diarrhœa with the passage of blood, and he had had two attacks since his discharge from the Royal Alexandra Hospital for Children. He had been admitted to the Royal North Shore Hospital of Sydney in June, 1950, during the second of the two attacks, which had lasted since January, 1950. He complained of anorexia, listlessness, and the passage of blood and mucus with diarrhœa. He had one to two motions every twenty-four hours, and the attacks were accompanied by general abdominal pain and tenderness. Sigmoidoscopic examination revealed that the surface of the bowel mucosa was congested and bleeding and covered with small, irregular, shallow ulcers. *Per rectum* the mucosa felt thickened. The hæmoglobin value was 63%, and the erythrocytes numbered 4,460,000 per cubic millimetre, with severe pallor of the cells and poikilocytosis. The leucocytes numbered 17,400 per cubic millimetre, 83% being lymphocytes, 10% monocytes, 5% neutrophile cells and 2% band forms. X-ray examination after a barium meal revealed that after six hours the stomach was practically empty and the jejunum was normal. The proximal part of the ileum appeared to be slightly dilated, and the terminal part of the ileum could not be visualized. The alimentary tract was almost completely empty in twenty-four hours, but the whole of the colon lacked haustration and normal mucosal pattern, and areas of narrowing were seen throughout its extent. The appearance of the colon was suggestive of severe ulcerative colitis. The chest appeared normal on radiological examination. Examination of the fæces revealed no evidence of parasites or of pathogenic organisms. Examination for *Mycobacterium tuberculosis* was still proceeding. The benzidine test provided evidence of the presence of occult blood. The result of a Mantoux test was negative. The administration of one litre of blood produced a considerable improvement in the hæmoglobin value of the patient's blood. Treatment was begun with aureomycin, 250 milligrammes being given every four hours. Vitamins *B* and *C* were also given parenterally. Immediately the temperature, which had been rising to 99° or 100° F. in the evening, became normal. Three weeks after the institution of aureomycin therapy, the patient was discharged from hospital, and at that stage was passing one formed stool each day, with no blood or mucus. His hæmoglobin value was 90%, the erythrocytes being of various sizes, shapes and staining qualities. The leucocytes numbered 18,600 per cubic millimetre, 68% being lymphocytes, 18% neutrophile cells, 7% eosinophile cells, 5% band forms, 6% monocytes and 2% basophile cells.

Carotid Body Tumour.

Dr. Lowenthal next showed two patients who had been suffering from carotid body tumour. The first patient, a married woman, aged sixty-five years, had been admitted to hospital in July, 1949, complaining of the presence of a lump in her neck for eighteen months, change in her voice for nine months and coughing when she pressed on the lump. She was found to have an oval, flat tumour, measuring three-quarters of an inch by half an inch, above the bifurcation of the common carotid artery. It appeared to be fixed to the artery and had a transmitted pulsation. Her pulse rate was 92 per minute, and the pulse was regular in timing and amplitude. The blood pressure in her right arm was 198 millimetres of mercury, systolic, and 100 millimetres, diastolic, and in her left arm 210 millimetres of mercury, systolic, and 115 millimetres, diastolic. An occasional split first heart sound was heard at the apex. Through an oblique incision in the left side of the neck the carotid sheath was opened and the tumour was removed after separation from neighbouring structures. It was very vascular, and appeared to be in continuity with the sympathetic trunk. The tumour, which measured five centimetres by two centimetres, was a carotid body tumour, histologically benign in appearance. The patient made a satisfactory recovery.

The next patient was a man, aged seventy-three years, who had been admitted to hospital in December, 1949, complaining of the presence of a lump on the left side of his neck for three years, a husky voice for one year and dyspnœa on effort for several years. He had an ill-defined tumour beneath the upper third of the right sterno-mastoid muscle. It was not fixed and not tender. The patient's blood pressure was 120 millimetres of mercury, systolic, and 80 millimetres, diastolic. The honorary ear, nose and throat surgeon reported diminished movement of the right vocal cord, and suggested a biopsy of the mass in the neck. Tests for syphilis gave negative results, the urine was sterile, and the blood urea content was within normal limits. Through a lateral vertical incision in the side of the neck, a lymph node was removed from the surface of the tumour and the tumour itself excised. The pathologist reported that the lymph node was normal. The cut surface of the tmour consisted of tissue of moderate consistency, with some jelly-like tissue between lobules of firmer tissue. Under the microscope it was found to be composed of large cells of indefinite outline with pale cytoplasm and large, fairly pale nuclei, lying in groups in a vascular stroma of fibrous tissue. The appearance was consistent with that of a carotid body tumour. When the patient was discharged from hospital nearly one month later, he still had a husky voice.

Chronic Ulcer of Foot due to Acid-Fast Organism.

DR. ERIC GOULSTON showed a wharf-labourer, aged forty-two years, who had been in the islands during the war. In 1946 the patient had suffered from an abrasion of the left foot, which appeared to heal; but a month later a scab appeared and separated, leaving a shallow ulcer with undermined edges, tending to spread while healing in its older parts. The patient was treated with sulphonamides and various local applications. The results of serological tests for syphilis were negative. In April, 1948, the patient had been referred to the School of Public Health and Tropical Medicine, University of Sydney, in the belief that the ulcer might be due to leprosy. Ulceration was then present in four areas, the largest being four inches across, with pigmentation and scar tissue, and adherent to the fibula. No acid-fast bacilli were found in smears, and no typical tuberculous tissue could be found microscopically. The result of guinea-pig inoculation was negative, but the organism was transmitted through successive generations of rabbits and possums. The ulcer was excised, and the patient was treated with 10% PAS and penicillin. By June, 1949, the area had healed. In November, 1949, an inflammatory area appeared on the dorsum of the left foot. Streptomycin-sensitive organisms were found in it, and the patient was referred for streptomycin therapy to the Royal North Shore Hospital of Sydney, to which he was admitted on January 12, 1950. His condition improved slowly, the local treatment including removal of sloughs, the application of Unna's paste, propamidine and a plaster of Paris cast, and the general treatment including the administration of streptomycin, penicillin, PAS and calciferol. The purpose of the plaster of Paris cast was to exclude *dermatitis artefacta*. On April 19, 1950, the ulcer was excised, and examination after Ziehl-Neelsen staining revealed the presence of acid-fast bacilli. The microscopic picture was that of typically tuberculous granulation tissue. X-ray examination revealed no periosteal or bony involvement. "Monacrin" emulsion and "Lux" baths were introduced into the local treatment. The serial examination of smears revealed the presence of *Bacillus pyocyaneus*, but no acid-fast bacilli. By April 24 the ulcer appeared healthy, and a split skin graft was applied from the thigh. Subsequent healing was satisfactory, propamidine cream having been used locally. The X-ray appearances in the patient's chest, the blood urea content and the temperature and pulse rate records were normal throughout the investigation. The result of a Mantoux test was positive. Dr. W. B. Kirkland, of the School of Public Health and Tropical Medicine, had suggested that the organism was identical with that described by McCallum in 1948 in his paper entitled "A New Mycobacterial Infection in Man".

Chemical Stenosis of the Œsophagus.

Dr. Goulston's next patient, a girl, aged seventeen years, had been first admitted to the Royal North Shore Hospital of Sydney on January 10, 1950, with a history of having swallowed caustic soda at the age of six years, with resultant œsophageal stricture. Several operations had been performed, but the patient could not swallow any liquid or solid, being fed through a gastrostomy tube. She was edentulous. X-ray examination with the swallowing of a barium bolus indicated the presence of complete œsophageal stricture about two inches below the aortic arch at the level of the seventh cervical vertebra. During the post-operative period partial collapse of the left lung occurred, but after bronchoscopy progressive reexpansion

took place. The diet was gradually built up until light solid foods were being swallowed successfully. On three occasions the patient found that food became caught in her throat, and œsophagoscopy and aspiration were necessary to give relief. Each time an incomplete stricture of the œsophagus was found 18 centimetres from the incisor teeth. X-ray examination revealed a narrow constriction at the level of the diaphragm, requiring about six inches' head of pressure to enable barium to pass into the abdominal portion of the stomach. An unsuccessful attempt was made to get the patient to swallow a small lead weight on a thread. An attempt was made to dilate the stricture from below through the gastrostomy wound, whilst simultaneously an œsophageal speculum was used from above, but this was unsuccessful because of inflammation of the gastric mucosa. It was decided to attempt this operation again when the inflammation had subsided. In April, 1950, œsophagoscopic examination was again carried out, and an impassable complete cicatricial obstruction was found at about the level of the diaphragm. An approach was then made simultaneously from above and below, communication was established, and a five-inch length of catheter was inserted on a loop of silk thread. Swallowing then became possible. A length of catheter of larger bore was later substituted, and the patient became able to swallow liquids, then semi-solids, and then solids such as eggs, biscuits, bread and rabbit. She was discharged from hospital in May, 1950, with the thread and catheter *in situ*. Dr. Goulston said that she was an intelligent girl and was able to adjust the position of the catheter when necessary. It was intended to replace the catheter by lengths of increasingly large bore until it could be dispensed with altogether.

Carcinoma of the Ampulla of Vater.

Dr. Goulston's last patient, a man, aged forty-five years, had been admitted to hospital in September, 1949, with a history of painless intermittent jaundice for eight months. He was very jaundiced, but otherwise in apparently good condition. His appetite was good, flatulence was slight, he was not upset by fatty foods, he had vomited only three times in the nine months and he was almost normal in weight. The liver edge was just palpable. Slight tenderness and muscular guarding were present over the gall-bladder area; otherwise the results of physical examination were negative. The results of biochemical tests indicated that the jaundice was of obstructive type. The serum bilirubin content was 17·8 milligrammes *per centum*; in the hippuric acid test 33% of normal excretion was obtained. The result of the cephalin cholesterol flocculation test was negative, the serum alkaline phosphatase content was 16·5 units, the results of tests for syphilis were negative, the hæmoglobin value of the blood was 70%, and the erythrocytes numbered 3,700,000 per cubic millimetre. The fæcal fat content was increased. No gall-stones were seen radiologically. After the administration of vitamin *K* and blood transfusion, laparotomy was carried out and a carcinoma of the ampulla of Vater was found. The diagnosis was later confirmed histologically. The duodenum and head of the pancreas were removed, the common bile duct was anastomosed to the jejunum and end-to-side gastro-jejunostomy was performed. Post-operative treatment included the intravenous administration of serum, blood and dextrose-saline solution. The patient was also given bile salts, "Synkamine", pancreatin, ascorbic acid, "Vivex" and methionine. During convalescence the patient developed a pancreatic fistula and had a period of vomiting; but he was free of both those complications and was walking about three weeks after operation. He was discharged from hospital on October 23, 1949, receiving a special diet including pancreatin. In February, 1950, his local doctor had reported that the patient was symptomless, had a good appetite and digestion and had gained about two stone in weight.

Buerger's Disease.

DR. C. H. WICKHAM LAWES showed a man, aged forty-seven years, who had first consulted him in February, 1949, complaining of cramps in the left leg after walking from 100 to 150 yards, with attacks of coldness and blanching of the leg and foot occurring for the previous twelve months. Examination of the patient revealed that the peripheral pulses in the legs were not palpable, blanching occurred on elevation of the limbs, the patient's blood pressure was 140 millimetres of mercury, systolic, and 85 millimetres, diastolic, and the claudication distance when the patient walked up a slight slope was 100 yards. The patient attended the out-patient department for some months and had various forms of treatment, including Buerger's exercises, intermittent venous occlusion and the administration of vitamin *E*, testoviron, "Etamon" and "Priscol". "Etamon" alone brought alleviation of symptoms. In December, 1949, the patient had a sudden attack of pain and coldness in the right leg with the onset of claudication, as well as attacks of blanching. His symptoms were then more severe than in his left leg. In January and February, 1950, section was performed first of the right femoral vein and then of the left femoral vein below the profunda vein. Some improvement resulted, but "Etamon" still produced an increased claudication distance. In March, 1950, a lumbar sympathetic block was carried out, and this improved the claudication distance considerably. Subsequently right and left lumbar sympathectomy was carried out. After the right lumbar sympathectomy the patient suffered from a small pulmonary infarct, and also developed a dynamic ileus after operation. After the left lumbar sympathectomy he had mild abdominal distension on the following day, but was given one millilitre of "Prostigmin" every two hours for five doses, which prevented ileus. At the time of the meeting both the patient's limbs were warmer, and the claudication distance was more than doubled. Dr. Lawes pointed out that the first special point in the case was the failure of many common forms of treatment to give relief; they were of value only in mild cases. The second point was the value of "Etamon" and lumbar sympathetic block as indications of the effect to be expected from sympathectomy. The third point was that certain risks accompanied the operation of lumbar sympathectomy.

Raynaud Phenomena.

Dr. Lawes's second patient was a woman, aged sixty-three years, who had complained of ulcers of the legs, deadness of the hands and feet, weakness, and spots on the tongue and skin. When examined in August, 1949, she had been found to have Raynaud phenomena, secondary anæmia, chronic ulceration of the legs, hæmorrhagic telangiectasia and raised systolic blood pressure. The anæmia and ulcers of the legs responded to hospital treatment, but the ulcer of the leg had not yet healed. "Priscol" had been administered for one month in a dosage of 25 milligrammes three times a day. Other features of the case were, firstly, the fact that the Raynaud phenomena and ulcer had not been affected by treatment with "Priscol", secondly, the sclerodermatous changes in the skin and superficial gangrene, thirdly, the arteriosclerosis and hæmorrhagic telangiectasia, which prevented a diagnosis of pure Raynaud disease, and fourthly, the fact that the patient was undergoing a six months' course of treatment with tocopherol in a dosage of 400 milligrammes per day.

Dr. Lawes then showed a girl, aged twenty-four years, who had been suffering from blueness and coldness of the limbs with swelling and varicose veins of the left leg. The following criteria of Raynaud's disease were present: firstly, the fact that the episodes of Raynaud's phenomena were excited by cold; secondly, the bilateral nature of the phenomena; thirdly, the absence of gangrene; fourthly the absence of other primary disease to cause the phenomena; fifthly, the fact that the phenomena had been present for more than two years. Other features of interest in the case were the fact that swelling of the left leg with varicosities had been present for four to five years, and that the patient had had an operation for recurrent dislocation of the patella in 1948. Dr. Lawes said that so far sympathectomy had not been considered necessary. The effect of "Priscol" was being tried, but the results had been inconclusive.

Perforating Ulcer of the Foot.

Dr. Lawes's last patient, a man, aged seventy-six years, had been admitted to hospital in 1947 with perforating ulcers of the feet. He had heaped callosity around the ulcers with exuberant granulations in the depths of the ulcers. His arterial circulation was satisfactory, and X-ray examination revealed sclerosis of the vessels of the lower limbs. Many forms of treatment had been tried, and success had been achieved with excision of the mass of callous skin around the ulcer, the application of felt rings round the ulcers, and the application of wool packing into the ulcers, which controlled granulation. The ulcers had been healed for twelve months at the time of the meeting.

Atypical Pneumonia.

DR. COTTER HARVEY showed a series of patients to illustrate atypical pneumonia, and demonstrated their X-ray films. The first patient, a man, aged twenty-five years, had been admitted to hospital on April 6, 1950, with a history that six days previously he had had a sudden sharp pain in the right lower lateral aspect of the chest accompanied by some shortness of breath. The symptoms had lasted for only a

short time. He was well for the next few days, but then developed malaise, fever, and a dull feeling in the right side of the chest, with some aching of the joints, especially the right knee joint. Examination of the respiratory system revealed no abnormality; but a slight degree of tachycardia was present, and a split first sound was heard at the mitral area. The right knee was free from fluid and local tenderness, and no deep calf tenderness was elicited. On the patient's admission to hospital his temperature was 100° F.; it fell to normal the next day, and remained so thereafter. The malaise, the dull feeling in the chest and the aching of joints disappeared in a few days. He was discharged from hospital on April 13.

Dr. Harvey's second patient, a young woman, aged twenty-one years, had been admitted to hospital on June 8, 1950; she complained of having felt tired and unwell for the previous ten days, and she had developed a cough with sputum. She had had a severe headache for one day at the commencement of the illness. On the patient's admission to hospital she was afebrile, but had a slight degree of tachycardia. No likely pathogens were grown from the sputum after forty-eight hours' incubation.

The third patient shown by Dr. Harvey was a man, aged twenty-five years, unmarried, who had been admitted to hospital on May 19, 1950; he gave a history of malaise for the previous nine days, cough with sputum for six days, and an hæmoptysis five days prior to his admission to hospital. The patient, who had been born in Greece, did not smoke tobacco or take alcohol. He had suffered from typhoid fever fifteen years earlier and from "pleurisy" six years earlier; X-ray films of his chest appeared normal. The hæmoptysis which he reported had occurred whilst he was lifting a heavy weight, and was apparently followed by an epistaxis. When examined on his admission to hospital, the patient said that he had suffered from night sweats and headache for one week. Consolidation of the upper half of the right lung and congestive signs at the base of that lung were found. During his stay in hospital the patient had received a total dose of 44 grammes of sulphadiazine, 156 grammes of PAS (12 grammes per day) and 7·0 grammes of streptomycin (0·5 gramme per day). All chemotherapy had been suspended on June 8. The patient's clinical condition was improving, although the improvement did not appear to have been related to the administration of specific therapy. The physical findings were unaltered. A number of investigations were carried out. Repeated examinations for acid-fast bacilli gave negative results, but the result of an attempt at culture was not yet available. Cold agglutinins were present in titres of 1:20 to 1:80. Bronchoscopic examination revealed no abnormality. On May 27 the honorary ear, nose and throat surgeon found that the epistaxis was coming from a vessel in Little's area on the right side; it was cauterized with trichloracetic acid. The larynx was normal. The patient reacted to the Mantoux test.

Bronchial Adenoma.

DR. BRUCE WHITE and DR. M. P. SUSMAN showed a man, aged thirty-nine years, who had been admitted to hospital on April 14, 1950. For four months he had suffered from periodic attacks of hæmoptysis with a productive cough, and for three months he had felt tired and had found that excessive exertion precipitated an hæmoptysis. Those symptoms became so acute that he gave up work. Investigation revealed that the hæmoptysis amounted only to staining of the sputum and was precipitated by exertion. The sputum was thick and tenacious, amounted to two ounces daily at the most, and was produced mainly in the mornings. The patient had lost no weight, and had noticed no dyspnœa, no hoarseness, no wheezing or stridor and no night sweats; he could recall no pyrexial attack. No abnormality was detected in the other systems and the family history was clear. In 1940 the patient had had several attacks of pleurisy; he had no history of contact with pulmonary tuberculosis.

On examination of the patient, no physical signs were detected. A bronchoscopic examination revealed no abnormality; no malignant tissue was seen. X-ray examination of the chest revealed an opaque area in the upper lobe of the left lung. The vital capacity was 3·4 litres. A blood count revealed no significant abnormality, and no acid-fast bacilli were found in the sputum. The pathologist reported the presence of reactive hyperplasia in hilar lymph glands, but no evidence of new growth. Tests for syphilis produced negative results.

Left pneumonectomy was performed on April 27. At operation the apex of the lung was found to be hard, and there were several apical adhesions with evidence of old pleurisy. Several enlarged lymph glands were removed at operation. It was necessary to divide the left vagus nerve and the left recurrent laryngeal nerve. Underwater drainage was instituted immediately after operation.

Physiotherapy and supportive coughing were instituted almost immediately after the operation, which was carried out under a penicillin and sulphadiazine "cover". On April 28 the cannula was removed after the patient had received three litres of blood and 0·5 litre of serum. On April 29 a further bronchoscopic examination was made, because of the presence of numerous râles and poor entry into the base of the right lung; a moderate amount of mucopurulent secretion was aspirated. From May 1 to 31 chest aspiration was required; 25 ounces of old frank blood were aspirated, and every third day 200,000 units of penicillin were instilled intrapleurally. On May 10 the initial pneumoperitoneum was instituted, and a fluoroscopic examination was made; the left cupola was found to move. Left phrenic crush was carried out. On May 21 the last "fill" of 1000 millilitres was given. The patient's post-operative course was satisfactory, the only complication being hoarseness due to division of the left recurrent laryngeal nerve. The patient was discharged from hospital, recovered, on June 1.

Chylothorax.

DR. BRUCE WHITE and DR. IAN MONK presented a single woman, aged forty-nine years, who had been on the stage all her life until twelve months before the meeting, when she took on clerical duties. At that time she began to complain of fatigue, but thought that it was due to the change of occupation. Whilst on the stage the patient had been subject to numerous falls, and her occupation involved a considerable amount of singing. Two years before the meeting she had had a trip to Japan as part of an entertainment unit, and during that time had had two attacks of severe bronchitis. She had no history of contact with pulmonary tuberculosis. In February, 1950, she began to notice dyspnœa on moderate exertion, and was admitted to hospital, where chyle-stained fluid was aspirated from the right pleural cavity, approximately two pints being removed every second day. In May, 1950, a bronchoscopic examination was made, but no bronchial abnormality was found. A pronounced expiratory wheeze with no apparent cause was noticed. There was practically no air entry on the right side. A bronchoscopic examination on the right side revealed normal visceral and parietal pleura, collapsed middle and lower lobes and a lower lobe adherent all along the mediastinum. Just behind the apex of the lower lobe an area could be seen from which chyle appeared to be coming. Forty ounces of chylous fluid were removed. On May 18, 1950, right thoracotomy was carried out with ligation of the thoracic duct. When the chest was opened about 20 ounces of chyle were aspirated from the pleural cavity, and a tiny pin-point area was seen, where chyle was escaping into the pleural cavity just behind the inferior pulmonary ligament and about 1·5 inches above the diaphragm. A longitudinal ridge was seen extending from the point where the azygos vein joined the vertebral column to a point two inches above the diaphragm. The azygos vein was found to be involved in that mass. The pleura was incised just beyond the inferior pulmonary ligament in the region of the leak. It was abnormally thickened and inelastic. The tissues were matted together as if they had been previously inflamed. No normal anatomical structure could be seen, although several vessels were ligated. It was then found that what was thought to be the right margin of the aorta was in fact a large sausage-shaped tumour about four inches in length surrounding the azygos vein. It was composed of softish, firm and friable tissue, whitish in appearance and avascular. It resembled a curd of milk in appearance and consistency, and was considered to be fatty deposit from the chylous effusion. When traced down, it was seen to end in the region where the leak into the pleura had been found. Accordingly the right side of the aorta was exposed where it passed through the diaphragm, the anterior part of the vertebral column was dissected bare, and all tissues in that corner were removed after ligation and division. It was thought that that should include the thoracic duct. About half-way through the operation the patient's heart stopped beating, but strong aeration of the lung and massaging of the heart twice restored its normal beat within thirty seconds. The patient's convalescence was satisfactory until it was noticed that there was poor air entry into the base of the left lung. Aspiration from the area produced about 20 ounces of blood-stained fluid. X-ray examination showed the presence of left basal atelectasis. The patient also complained of considerable post-operative right-sided pain, but there was no evidence of return of the chyle, and the patient was discharged from hospital, recovered, on June 10, 1950.

Bronchogenic Carcinoma.

DR. C. G. BAYLISS and DR. IAN MONK then presented a man, aged sixty years, who had been admitted to hospital on April 30, 1950, with a history of tiredness, lassitude and dyspnœa for five months, cough and sputum for three months, and hæmoptysis for six weeks. He had had no loss of weight, hoarseness, night sweats or history of pyrexial attacks. Examination of the patient revealed inspiratory stridor on the right side, but no other physical signs of significance. Bronchoscopic examination revealed that about half to three-quarters of the right stem bronchus wall was bulged in on the postero-medial side by a mass which was very hard and immobile, and reduced the lumen to about half its normal size. The right upper lobe bronchus opening was partly occluded by a mass which bled very easily. The appearances were suggestive of a cancer of the right upper lobe bronchus, and biopsy revealed the presence of a squamous-celled carcinoma. On May 4, 1950, right pneumonectomy was carried out with a right phrenic crush. Apart from the occurrence of a bronchial fistula on the twentieth day after operation, which closed after the institution of pneumoperitoneum, the convalescence was satisfactory, and the patient was discharged from hospital on June 14, 1950.

(To be continued.)

Correspondence.

FOOD FOR BRITAIN.

SIR: I venture to ask for the hospitality of your columns in order to tell members of the New South Wales Branch of the British Medical Association how deeply grateful the Committee of the Royal Medical Benevolent Fund are for the gift parcels which have been received regularly ever since 1947. The number of parcels received now amounts to thousands.

The beneficiaries of the fund are not only deeply appreciative, but they are also very touched by the kind thought of colleagues so far away. At the headquarters of the fund we are constantly receiving letters of thanks, and requests that those thanks shall reach the generous donors.

Many of your readers are among those who have taken part in this generous gesture, and I want them to know that their action has warmed our hearts and bound us closer to them.

Yours, etc.,

70 Portland Place, W.1, London, October 17, 1950.

WEBB-JOHNSON.

Obituary.

CHARLES FITZMAURICE HARKIN.

WE regret to announce the death of Dr. Charles Fitzmaurice Harkin, which occurred on September 25, 1950, at Chiltern, Victoria.

HANNAH MARY HELEN SEXTON.

WE regret to announce the death of Dr. Hannah Mary Helen Sexton, which occurred recently in London.

Australian Medical Board Proceedings.

QUEENSLAND.

THE undermentioned have been registered, pursuant to the provisions of *The Medical Acts*, 1939-1948, of Queensland, as duly qualified medical practitioners:

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED OCTOBER 14, 1950.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.[2]	Australian Capital Territory.[2]	Australia.[2]
Ankylostomiasis	*	..	..	..	..	..	..	..	..
Anthrax	*	..	..	..	..	..	..	..	..
Beriberi	*	*	*	*	*	*	..	*	..
Bilharziasis	*	..	..	..	..	..	..	..	..
Cerebro-spinal Meningitis	..	2(2)	1	..	..	..	..	..	3
Cholera	..	..	..	..	..	..	..	..	..
Coastal Fever(*a*)	*	*	..	*	*	*	*	*	..
Dengue	*	*	*	*	*	*	..	*	..
Diarrhœa (Infantile)	..	..	6(3)	..	..	..	..	..	6
Diphtheria	7(3)	..	7(2)	..	2(2)	1(1)	..	..	17
Dysentery (Amœbic)	*	..	..	..	..	..	..	..	..
Dysentery (Bacillary)	*	..	4(4)	..	..	..	..	..	4
Encephalitis Lethargica	..	..	..	..	..	..	..	..	..
Erysipelas	*	*	*	..	*	*	..	..	..
Filariasis	*	..	..	..	..	..	..	..	..
Helminthiasis	*	1(1)	*	*	*	*	*	*	1
Hydatid	*	..	*	*	..	*	*	..	..
Influenza	*	*	*	..	*	*	..	*	..
Lead Poisoning	*	*	..	*	*	*	*	*	..
Leprosy	..	..	..	..	..	..	..	..	..
Malaria(*b*)	*	..	..	..	..	..	..	..	..
Measles	*	*	*	498(288)	*	*	..	..	498
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	7(2)	2(2)	1	3(3)	..	1	..	..	14
Psittacosis	*	..	*	..	*	*	*	*	..
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella(*c*)	*	*	..	*	1(1)	*	..	..	1
Scarlet Fever	12(7)	17(10)	21(16)	10(7)	1	1	..	..	62
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	*	..	2	*	1(1)	*	*	*	3
Trachoma	*	..	*	*	*	*	*	*	..
Tuberculosis(*d*)	21(20)	34(25)	27(19)	11(11)	14(7)	4(2)	..	..	111
Typhoid Fever(*e*)	..	1(1)	..	1(1)	..	..	..	..	2
Typhus (Endemic)(*f*)	..	..	..	..	..	..	..	..	..
Undulant Fever	..	2(1)	..	..	..	..	..	..	2
Weil's Disease(*g*)	*	*	..	*	*	*	*	*	..
Whooping Cough	*	*	*	1(1)	*	*	..	..	1
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] The form of this table is taken from the *Official Year Book of the Commonwealth of Australia*, Number 37, 1946-1947. Figures in parentheses are those for the metropolitan area.

[2] Figures incomplete owing to absence of returns from the Northern Territory and Australian Capital Territory.

* Not notifiable.

(*a*) Includes Mossman and Sarina fevers. (*b*) Mainly relapses among servicemen infected overseas. (*c*) Notifiable disease in Queensland in females aged over fourteen years. (*d*) Includes all forms. (*e*) Includes enteric fever, paratyphoid fevers and other Salmonella infections. (*f*) Includes scrub, murine and tick typhus. (*g*) Includes leptospiroses, Weil's and para-Weil's disease.

Singer, Ernest, M.D. (German University, Prague), 1923, registered in accordance with Section 20 (1) (c) and (d), c.o. the Queensland Institute of Medical Research, Brisbane.

Thoms, John Allan, M.B. (Univ. Sydney), 1927, 35 Dornoch Terrace, Hill End, Brisbane.

The following additional qualification has been registered:

Macfarlane, Walter Victor, c.o. Department of Physiology, University of Queensland, Brisbane, M.D. (Univ. New Zealand), 1940.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Rothery, Donald Edward, M.B., B.S., 1945 (Univ. Sydney), Bygoo Street, Ardlethan, New South Wales.

Gray, Geoffrey George, M.B., B.S., 1947 (Univ. Sydney), 107 O'Sullivan Road, Bellevue Hill.

Carr, Kenneth Allan, M.B., B.S., 1950 (Univ. Sydney), 30 Ravenswood Avenue, Randwick.

Dixon, Ian, M.B., B.S., 1950 (Univ. Sydney), Hornsby District Hospital, Hornsby.

Gilbert, Elaine Therese, M.B., B.S., 1950 (Univ. Sydney), Bathurst District Hospital, Bathurst.

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 61, of October 12, 1950, and Number 62, of October 19, 1950.

CITIZEN NAVAL FORCES OF THE COMMONWEALTH.

Royal Australian Naval Volunteer Reserve.

Appointments.—Philip William Van Gelderen is appointed Surgeon Lieutenant-Commander, with seniority in rank of 24th July, 1950, dated 21st August, 1950. Richard Kernan Newing is appointed Surgeon Lieutenant, with seniority in rank of 18th April, 1946, dated 8th August, 1950.

AUSTRALIAN MILITARY FORCES.

Citizen Military Forces.

Northern Command: First Military District.

Royal Australian Army Medical Corps (Medical).—1/43724 Major G. B. V. Murphy is appointed from the Reserve of Officers, and to be Temporary Lieutenant-Colonel, 20th June, 1950. To be Captain (provisionally), 30th August, 1950: 1/25222 Bruce Bruce-Smith.

Southern Command: Third Military District.

Royal Australian Army Medical Corps (Medical).—3/52176 Lieutenant J. A. Forbes is appointed from the Reserve of Officers, and to be Captain (provisionally), 9th August, 1950.

Central Command: Fourth Military District.

Royal Australian Army Medical Corps (Medical).—The provisional rank of 4/35205 Major J. M. McPhie is confirmed. 4/31911 Captain F. E. Welch was seconded whilst undergoing post-graduate studies in the United Kingdom from 26th August, 1949, to 1st August, 1950.

Tasmanian Command: Sixth Military District.

Royal Australian Army Medical Corps (Medical).—The provisional appointment of 6/9029 Captain G. B. Watkins is terminated, 8th August, 1950.

Reserve Citizen Military Forces.

Royal Australian Army Medical Corps.

2nd Military District: To be Honorary Captain, 9th August, 1950.—George Bertram Watkins.

5th Military District: To be Honorary Captain, 23rd August, 1950.—Alan Alison Barr.

ROYAL AUSTRALIAN AIR FORCE.

Permanent Air Force: Medical Branch.

The probationary appointments of the following Flight Lieutenants are confirmed: J. W. L. Atkinson (034056), D. H. Prentice (051149).

The following Flight Lieutenants (Temporary Squadron Leaders) are promoted to the rank of Squadron Leader, 1st March, 1950: J. B. Craig (05799), L. R. Trudinger (033059), G. A. Leyland (04397), M. C. Clarke (011321).

Diary for the Month.

Nov. 7.—New South Wales Branch, B.M.A.: Organization and Science Committee.
Nov. 10.—Queensland Branch, B.M.A.: Council Meeting.
Nov. 13.—Victorian Branch, B.M.A.: Finance, House and Library Subcommittee.
Nov. 14.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
Nov. 15.—Western Australian Branch, B.M.A.: General Meeting.
Nov. 16.—Victorian Branch, B.M.A.: Executive Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney)—All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

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